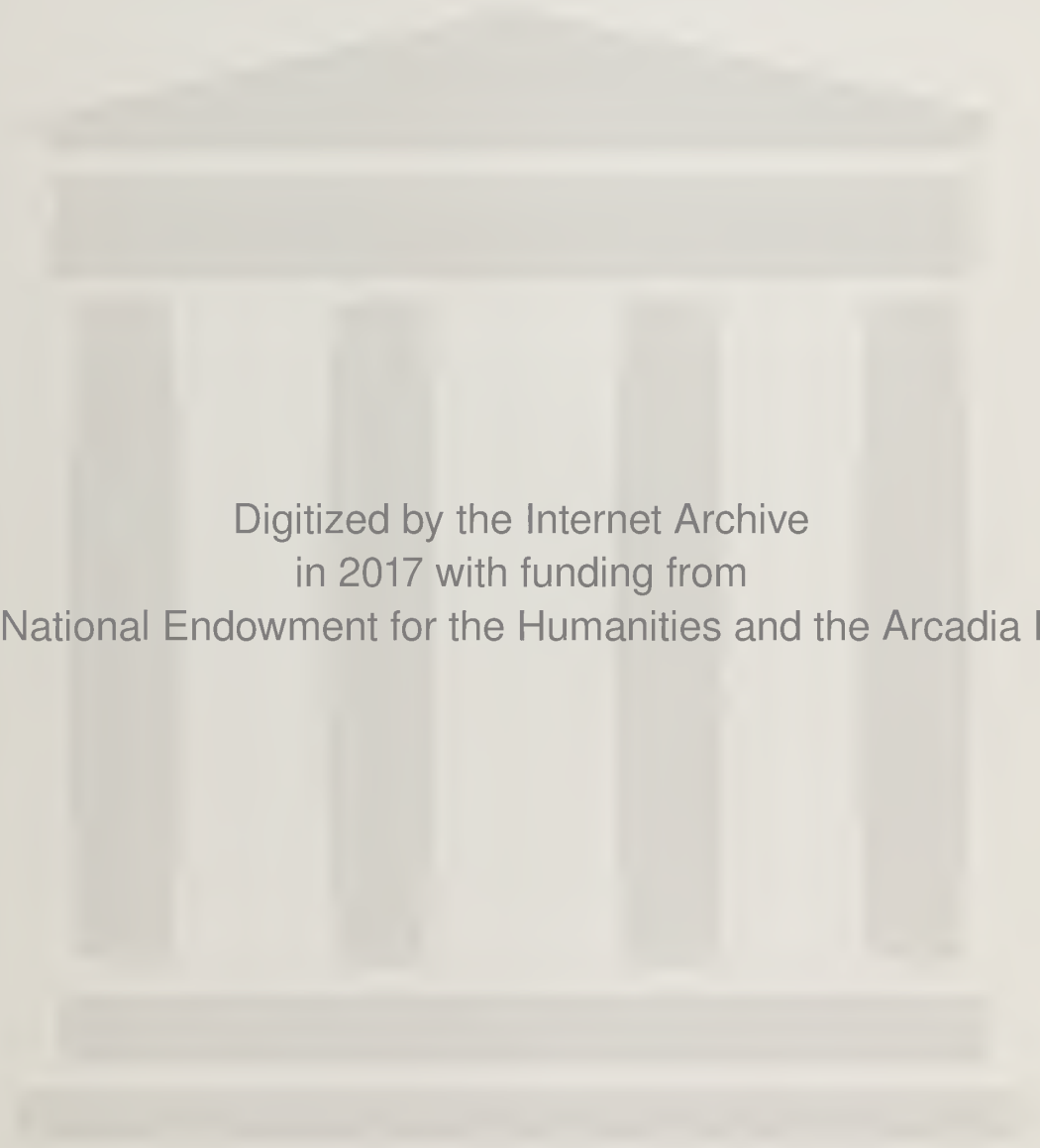
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Breast self-examination:

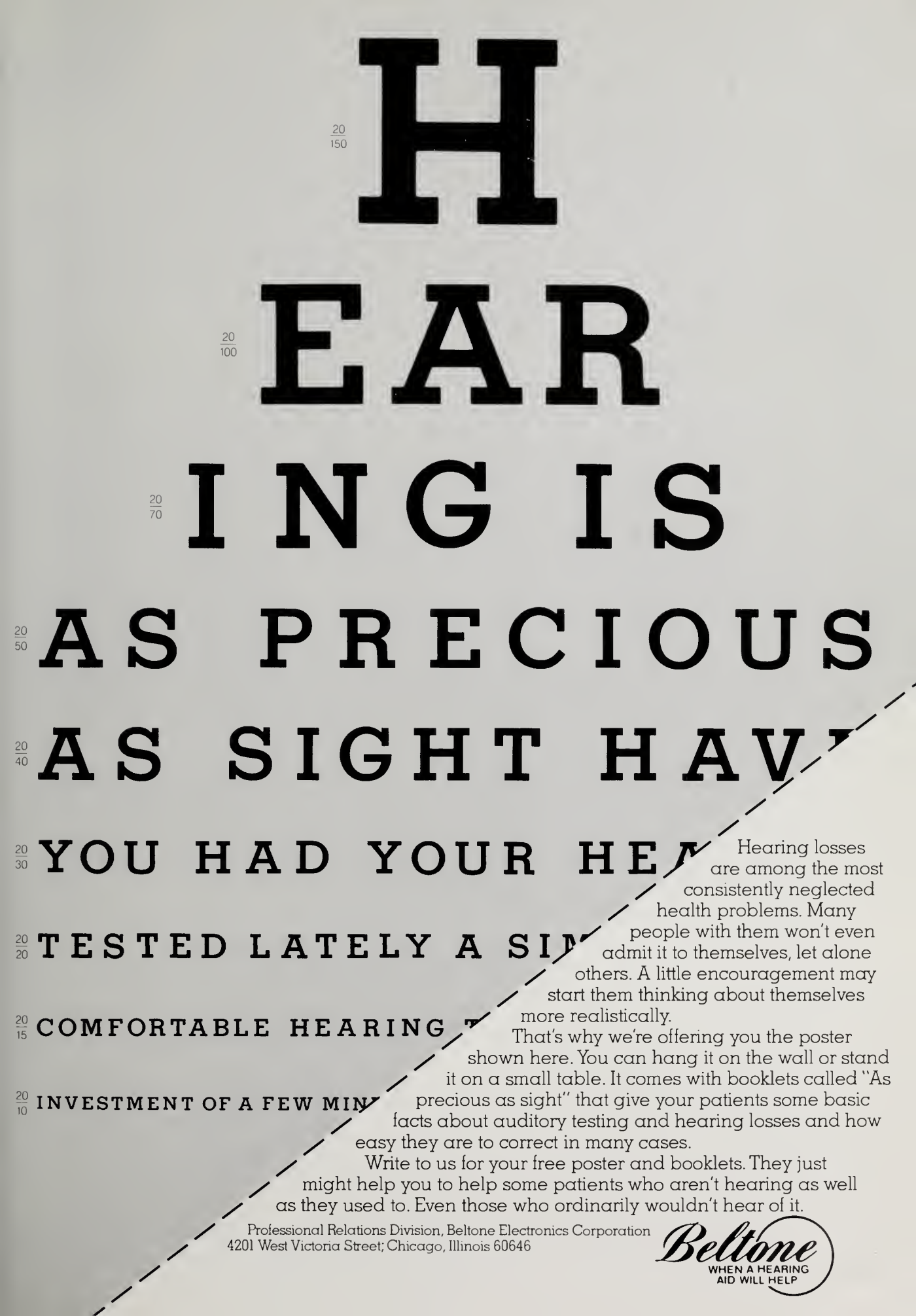
KEY ROLE OF THE PHYSICIAN

item:	**Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.**
item:	**Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, *fewer than 1 in 5* women practice BSE, and *only half* have an annual breast examination by a physician.**
item:	**Only 35% of all women polled reported that a *physician* had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.**
item:	***But,* among women who received personal instruction from their physicians, the overwhelming majority *(92%)* practiced BSE during the preceding year.**

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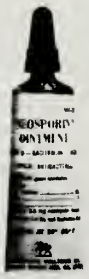
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Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing **CONTRAINDICATIONS:** Not for use in the eyes or external ear canal if the eardrum is perforated This product is contraindicated in those individuals who have shown hypersensitivity to any of the components **WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patien' has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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– A NUESTROS PATROCINADORES –

En este año a punto de terminar, la Junta Editora desea expresar su agradecimiento a nuestros patrocinadores del Boletín de la Asociación Médica de Puerto Rico, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos. Son éstos proveer un medio para la publicación de artículos científicos de nuestros médicos, informar a nuestros lectores de problemas médicos de importancia, proporcionar vías de comunicación para expresar puntos de vista; tanto oficiales como de índole personal, estimular liderato médico para la solución de nuestros problemas; en fin, lograr una revista de actualidad que refleje la calidad de la medicina Puertorriqueña.

Agradecemos la ayuda y apoyo de nuestros patrocinadores.

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In this year about to end, the Editorial Board recognizes with gratitude the aid provided by those advertising in the Boletín de la Asociación Médica de Puerto Rico, whose support permits the fulfillment of our objectives. These are to provide the medium for publication of scientific articles by our physicians, to keep our readers informed of diverse medical problems of importance, to provide communication means for the expression of different points of view, to stimulate medical leadership for the solution of our problems, in short, to produce a journal which will reflect the quality of Puerto Rican medicine.

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BRIEF SUMMARY
Indications: Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone; routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May be additive or potentiative of the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Usage in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in cord blood and breast milk. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis; dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia; purpura, photosensitivity, rash, urticaria, necrotizing angiitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg. (white, scored) and 50 mg. (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6.

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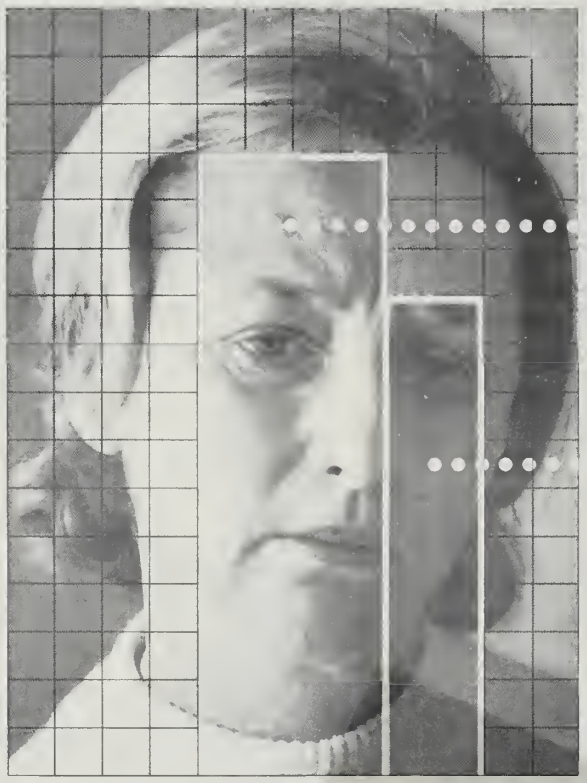
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Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

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Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium® (diazepam) IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic anxiety states with associated depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.
If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.
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ADVERSE REACTIONS
Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE
Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED
Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment,* 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. *Lotion,* 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream,* 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment,* 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

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Noticias 1

THE NERVE THAT CARRIES SORE THROAT PAIN.



THE SORE THROAT GARGLE THAT BLOCKS IT.

The ninth cranial nerve. That's what doctors call the telegraph line that carries sore throat pain to your brain.

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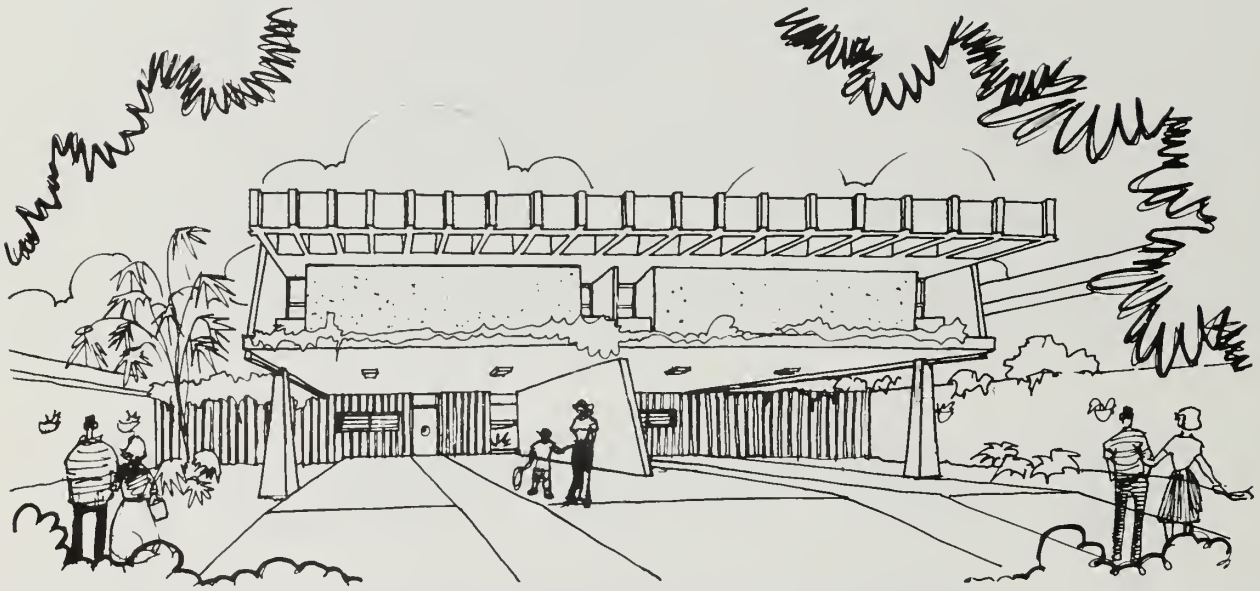
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Se van a construir estas dos magníficas residencias en un estupendo terreno en El Señorial. Los planos y el Rendering a colores se pueden ver en la oficina del Arq. Tony Martin, en el Edificio Midtown, Muñoz Rivera 421, Hato Rey, oficina 808, o llamar al Arquitecto, al teléfono 763-2777 durante el día o 763-7097 durante la noche.

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NUEVO METODO PARA EL USO COMBINADO DE CICLOPLEGICOS DE ACCION CORTA

Manuel N. Miranda, MD

Los cicloplégicos son de gran utilidad no sólo para determinar adecuadamente la hiperopia y el astigmatismo hiperópico, sino que también para no sobrecorregir la miopía y la astigmia miópica. Nos brindan el único método que nos permite medir adecuadamente el grado de parálisis de la acomodación y descubrir espasmos de la acomodación.

En la actualidad contamos con un grupo de cicloplégicos de acción corta que nos permite practicar una refracción adecuada al paciente sin causarle muchas molestias. Los tres que más se usan son ciclopentolato, tropicamida y homatropina.

Cicloplégicos Disponibles

Tropicamida, ciclopentolato y homatropina son los llamados cicloplégicos de acción corta porque tienen tiempos de inducción y recuperación relativamente cortos. Las tres drogas son parasimpatolíticas, causan parálisis del esfíncter del iris y del músculo ciliar entorpeciendo o bloqueando la acción de la acetilcolina sobre los receptores al nivel de las células musculares.

Tropicamida (Mydriacyl) (1, 2, 3, 4) es un compuesto sintético, descrito químicamente como una amida del ácido trópico. Los Laboratorios Alcon lo fabrican y se expende en concentraciones de 0.5 por ciento y 1 por ciento. Solamente el 1 por ciento se usa como cicloplégico. La dosis es de una gota cada cinco minutos por dos veces. Produce efectos cicloplégicos máximos entre 20 y 35 minutos después de la última gota. El examen debe practicarse durante ese período ya que su acción máxima desaparece rápidamente. El período de recuperación de la cicloplegia es de 2 a 6 horas.

Ciclopentolato (Cyclogyl) (5, 6, 7) es un compuesto sintético, un ester soluble en agua, de una estructura química parecida a la de atropina. Los Laboratorios Alcon también lo fabrican y se expende en concentraciones de 0.5 por ciento, 1.0 por ciento y de 2.0 por ciento. Las tres concentraciones son cicloplégicas; la de 0.5 por ciento se utiliza en irises claros y la de 2.0 por ciento en irises pigmentados. La dosis media es de una gota en cada ojo. Produce efectos máximos entre 25 y 75 minutos después de su aplicación. El período de recuperación es de 6-24 horas.

Homatropina es un alcaloide que se obtiene por la condensación de tropina y el ácido mandélico. Se encuentra en el mercado en soluciones del 2 por ciento al 5 por ciento. La dosis de la solución al 2 por ciento es de una gota en cada ojo cada 10 minutos por 6 veces. Produce efectos máximos entre 40 y 90 minutos. Su período de recuperación es de 36 a 48 horas.

La acción cicloplégica del ciclopentolato (Cyclogyl) es superior a la de homatropina. Tiene un período de inducción más rápido, una duración más corta y una intensidad mayor. Para producir el mismo grado de cicloplegia que con ciclopentolato se necesita una dosis mayor de homatropina. Por consiguiente el ciclopentolato ha suplantado a la homatropina como agente cicloplégico.

La acción cicloplégica del ciclopentolato (Cyclogyl) es también superior a la de la tropicamida (8). Aunque el período de inducción de la tropicamida es más rapido que el del ciclopentolato, su período de acción máxima es demasiado corto (alrededor de 15 minutos) y desaparece rápidamente, mientras que el del ciclopentolato es más prolongado (alrededor de 50 minutos) y su acción máxima desaparece gradualmente. Esto nos permite suficiente tiempo para practicar un examen adecuado al paciente. Con tropicamida muchas veces cuando vamos a examinar el segundo ojo éste presenta una aco-

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De la Escuela de Medicina Universidad de Puerto Rico. *Presentado en el X Congreso Pan Americano de Oftalmología celebrado en el Hotel Caribe Hilton, San Juan, Puerto Rico, en abril de 1975.*

Favor de solicitar reimpresos a: Manuel N. Miranda, M.D., GPO Box D, San Juan, Puerto Rico 00936.

modación residual mayor que la del primer ojo.

Tropicamida produce una cicloplegia inadecuada en la mayoría de los pacientes menores de 20 años. Para producir el mismo grado de cicloplegia que con el ciclopentolato se necesita una dosis mayor de tropicamida.

Gettes (9) estudió los efectos cicloplégicos de la homatropina, tropicamida y ciclopentolato en grupos de pacientes con buena acomodación usando dos gotas de tropicamida al 1 por ciento, dos gotas de homatropina al 4 por ciento y una gota de ciclopentolato al 1 por ciento.

El estudio demostró que el ciclopentolato es el más efectivo; que tropicamida tiene un período muy corto de cicloplegia adecuada, y que la homatropina no sólo es el menos efectivo, sino que tiene un período de inducción mucho más prolongado.

Por consiguiente, ciclopentolato es el cicloplégico mejor que tenemos en la actualidad.

Sin embargo, en irises de color chocolate, pigmentados, es difícil lograr una cicloplegia adecuada aun con el uso de ciclopentolato.

Para producir una cicloplegia adecuada en irises pigmentados es necesario usar dosis repetidas del ciclopentolato al 1 por ciento o 2 por ciento.

El uso del 2 por ciento y de dosis repetidas del 1 por ciento ha producido en muchos pacientes, especialmente en niños o personas con historial de daño cerebral, reacciones tóxicas cerebrales (10, 11, 12, 13) tales como alucinaciones, ataxia, convulsiones, reacciones esquizofrénicas y otras reacciones psicóticas. Se hace mención frecuentemente sobre el parecido de la estructura química del ciclopentolato con substancias alucinogénicas tales como el ácido lisérgico.

Debido a la toxicidad del ciclopentolato en sobredosis, a que su efectividad en irises pigmentados u obscuros es menor, y a que en Puerto Rico alrededor del 20 por ciento de las personas tienen irises pigmentados, desde hace varios años comencé a utilizar con éxito, en estos pacientes, el uso combinado de una gota del 1 por ciento de ciclopentolato con una gota del 1 por ciento tropicamida (14).

A continuación les quiero informar los resultados de un estudio que hice en 1971 (15) sobre la acomodación residual, comparando la efectividad del 1 por ciento ciclopentolato con el uso combinado del 1 por ciento ciclopentolato y 1 por ciento tropicamida en ojos con diferentes colores de irises.

Estudio de Acomodación Residual

Practiqué ciento ochenticinco refracciones cicloplégicas consecutivas en pacientes dentro de los 7 y 36 años de edad excluyendo aquellos pacientes que no pudieron mejorarse a 20/20 en cada ojo o que presentaban anisometropía mayor de 1 dioptría o tenían ametropias fuertes.

Una gota de proparacaína (Ophthaine) al 0.5 por ciento se le echó en ambos ojos seguida segundos más tarde, por una gota de ciclopentolato (Cyclogyl) al 1 por ciento en ambos ojos también. Al ojo izquierdo, 25 segundos después del ciclopentolato, se le echó una gota de tropicamida (Mydriacyl) al 1 por ciento. El examen se practicó 30 o 40 minutos más tarde.

Para calcular la acomodación residual se usó una cartilla de prueba de lectura montada a 16 pulgadas en un refractor. Un lente de + 2.50 esférico se le puso sobre la corrección de distancia y se les pidió a los pacientes que leyeran en voz alta el párrafo más pequeño (J_1), Se le agregaron esferas negativas aumentando su potencia gradualmente en intérvalos de 0.50 D al principio y luego de 0.25 D al final, hasta que el paciente ya no pudo leer más. La prueba se llevó a cabo en cada ojo separadamente.

Resultados

El estudio demostró (ver Tabla) que en irises claros (azules, verdes, castaño claro y castaño mediano) ciclopentolato al 1 por ciento produjo cicloplegia adecuada (promedio de la acomodación residual fue 0.70 ± 0.24 D) 30 a 40 minutos después de la instilación en los ojos y que es prácticamente tan efectiva como el uso combinado de 1 por ciento ciclopentolato y de 1 por ciento tropicamida (promedio de la acomodación residual fue 0.66 ± 0.22 D). Es bueno notar que en todos los pacientes de irises claros el 1 por ciento ciclopentolato produjo 1.25 dioptrías o menos de acomodación residual. En el trabajo efectuado por Gettes en 1961 la mayoría de los pacientes, que tenían irises claros, tenía una acomodación residual entre 1.5 y 2.0 dioptrías. La diferencia de la acomodación residual entre el trabajo de Gettes y el mío probablemente se debió al hecho de que él no usó anestesia tópica antes de usar el ciclopentolato.

En irises obscuros (pigmentados, chocolate, etc.) la combinación de ambas drogas (promedio de la acomodación residual fue 0.77 ± 0.26 D) demostró ser práctica y significativamente superior al uso de ciclopentolato solo (promedio de la acomodación residual fue 2.22 ± 0.96 D). El uso combinado de ambas

TABLA
DISTRIBUCION DE PACIENTES POR COLOR DE IRIS Y ACOMODACION RESIDUAL EN DIOPTRIAS 30 A 40 MINUTOS DESPUES DE LA ADMINISTRACION DEL 1 POR CIENTO CICLOPENTOLATO EN O. D. Y 1 POR CIENTO CICLOPENTOLATO MAS 1 POR CIENTO TROPICAMIDA EN O. S.

Acomodación Residual (D)	1 Por ciento Ciclopentolato OD		1 Por ciento Ciclopentolato Más 1 Por Ciento Tropicamida OS	
	Irises Claros *	Irises Obscuros	Irises Claros *	Irises Obscuros
0.25	10	-----	11	2
0.50	43	-----	52	12
0.75	59	-----	56	12
1.00	23	-----	21	14
1.25	7	5	2	3
1.50	----	8	----	----
1.75	----	5	----	----
2.00	----	8	----	----
2.25	------	5	----	----
2.50	----	3	----	----
2.75	----	----	----	-----
3.00	----	2	----	----
3.25	----	2	----	----
3.50	----	2	----	----
3.75	----	----	----	----
4.00	----	1	----	----
4.25	----	----	----	----
4.50	----	1	----	----
4.75	----	----	----	----
5.00	----	----	----	----
5.25	----	----	---	----
5.50	----	1	----	----
TOTAL	142	43	142	43
Medio ± DE	0.70 ± 0.24	2.22 ± 0.96	0.66 ± 0.22	0.77 ± 0.26

** - Incluye irises azules, verdes, castaño claro y castaño mediano.*

drogas produjo una acomodación residual de 1.25 dioptrías o menos en todos los pacientes, mientras que el 1 por ciento ciclopentolato alcanzó este nivel en únicamente cinco de los 43 pacientes con irises obscuros.

De acuerdo con algunos, para que un agente cicloplégico sea efectivo debe de producir una acomodación residual de menos de 2.50 D; otros creen que el límite debe ser de 2.00 D; y otros que el 1.50 D o 1.00 D. Sí, todos están de acuerdo que mientras menor sea la acomodación residual más efectivo será el cicloplégico.

Ciclopentolato 1 por ciento usado solo, produjo una acomodación residual de

2.25 D o menos en 72 por ciento de los pacientes
1.75 D o menos en 41 por ciento de los pacientes
1.25 D o menos en sólo 11 por ciento de los pacientes

Conclusiones

1. Una gota de ciclopentolato al 1 por ciento, precedida de una gota de anestésico local, produce

cicloplegia efectiva en todos los irises claros a los 30 o 40 minutos.

2. El uso combinado de una gota de 1 por ciento ciclopentolato y de una gota de 1 por ciento de tropicamida, precedido por una gota de anestésico local, produce cicloplegia efectiva en todos los irises obscuros a los 30 o 40 minutos.

3. No se han producido efectos tóxicos con el uso de una sola gota de 1 por ciento ciclopentolato o con el uso combinado con una gota de tropicamida al 1 por ciento.

4. Otros oftalmólogos, entre ellos el doctor Robert D. Reinecke (16), han comprobado la efectividad del uso combinado de las tres drogas, proparacaína, ciclopentolato y tropicamida.

Resumen

Se compara la acción cicloplégica de los tres cicloplégicos de acción corta que más frecuentemente se usan en la actualidad y se presenta un nuevo método para el uso combinado de proparacaína, ciclopentolato, y tropicamida que es más efectivo y menos tóxico que el uso individual de las drogas.

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HORMONA TIROTROPA EN RECIEN NACIDOS E INFANTES JOVENES

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Los recién nacidos normales presentan un estado fisiológico de hipersecreción de hormonas tiroideas durante la primera semana de vida, especialmente durante las primeras 12 a 72 horas. Estos niveles se mantienen elevados durante el primer mes, nivelándose como las de adultos al 3 - 4 mes de vida (1-3).

En un estudio previo de niveles de captación en resina de T-3, tiroxina total e índice de tiroxina libre, sugerimos que dicha hipersecreción de hormonas tiroideas, después de las primeras 12 horas de vida, podría ser debida a hipersecreción de hormona ' tirotropa. Fisher y Odell (4) han demostrado que existe una marcada, pero transitoria, secreción de TSH durante los primeros 30 minutos de vida.

Motivados por estos hechos estudiamos en nuestra muestra patrón (sujetos del mismo estudio), los niveles circulantes de hormona tirotropa.

Sujetos y Métodos

Se estudiaron 13 recién nacidos varones y 12 hembras nacidas a término en el Hospital Dr. R. E. Betances del Centro Médico de Mayagüez. Se obtuvieron muestras, con el consentimiento de los padres, a las edades de 0 - 24 horas, 48-72 horas, 1 semana, 1 mes, 2 meses, 3 meses y 4 meses, realizando determinaciones de los niveles circulantes en plasma de hormona tirotropa. Representan éstas el mismo grupo de pacientes del estudio previo de hormonas tiroideas.

Se excluyeron del estudio los prematuros, niños de bajo peso al nacer, recién nacidos con complicaciones perinatales, y los hijos de madres con síndrome nefrótico, endocrinopatía o que recibían terapia hormonal.

Los niveles de hormona tirotropa circulante fueron determinados mediante técnica de radioinmunoensayo con doble anticuerpo (5). La radioactividad fue determinada con el Analizador Biogamma de tres canales de la casa Beckman. Debido al elevado costo de los reactivos reducimos la muestra patrón a 12 hembras y 13 varones. Todas las determinaciones se realizaron a la vez para evitar variaciones entre ensayos.

De la Sección de Endocrinología Pediátrica y Genética Médica del Hospital Dr. R. E. Betances, Centro Médico de Mayagüez.

Resultados

La Tabla I nos muestra los niveles de hormona tirotropa circulante en un sujeto varón y una hembra en los primeros seis meses de vida. Después del mes de edad estos valores caen dentro de los límites normales (para un adulto 0-10 mUI/ml) por lo que nuestro estudio se redujo a la evaluación del primer mes en el resto de los sujetos.

La Tabla II muestra los niveles de hormona tirotropa circulante en 12 hembras y 13 varones, de forma seriada, desde el nacimiento hasta el mes de edad. En las edades de 0-24 hrs., 48-72 horas, y una semana de vida los niveles de TSH son superiores en los varones a los de las hembras, siendo la diferencia estadísticamente significativa a un nivel de 0.05-0.025 en las primeras 24 horas de vida. De forma definitiva y evidente, se observa una diferencia enorme entre los niveles circulantes de TSH en las primeras 24 horas y las 48-72 horas, tanto en los varones como las hembras.

La evaluación de dos subgrupos en el período de edad de 0-24 horas nos revela datos interesantes. Evaluando los sujetos menores de 12 horas de edad, comparados con los mayores de 12, pero menores de 24 horas (irrespectivo del sexo), observamos que la secreción de TSH es definitivamente superior en las primeras 12 horas, siendo estadísticamente significativas a un nivel de 0.025 - 0.01. Al comparar los sexos (Tabla III). observamos que los niveles de TSH son superiores en los varones menores de 12 horas, e inferiores a las hembras en los varones mayores de 12 horas de edad. La diferencia entre sexos es estadísticamente significativa en los menores de 12 horas a un nivel de 0.025 - 0.01.

Discusión

La función tiroidea en niños ha sido objeto de varios estudios. Nuestro estudio previo mostró en una muestra seriada, de forma longitudinal, la evaluación contínua de la función tiroidea desde el primer día de vida hasta los 4 meses de edad, observando una diferencia signi-

TABLA I
NIVELES DE TSH EN LOS PRIMEROS 6 MESES DE VIDA EN UN VARON Y UNA HEMBRA

Edad	NIVELES DE TSH E. M. ♀	E. A. P. ♂
0-24 hrs.	31 mU.I./ml.	58 mU.I./ml.
48-72 hrs.	10.8	11
1 sem.	6.9	7.8
1 mes	11	6.8
2 meses	6.9	7.45
3 meses	5.45	6.3
4 meses	4.8	7.7
6 meses	3.85	4.8

TABLA II
NIVELES DE TSH EN 13 VARONES Y 12 HEMBRAS

EDAD		TSH (m.U.I./ml.) Hembras ♀	Varones ♂	Cálculos Estadísticos t	p
	$\bar{X}$	23.04	36.17		
0-24 hrs.	D. E.	11.31	21.13	1.817	0.05 - 0.25 *
	F	0.42 - 45.66	0 - 78.43		
	$\bar{X}$	6.19	8.37		
48-72 hrs.	D. E.	2.44	3.62	1.679	0.10 - 0.05
	F	1.31 - 15.10	1.13 - 15.61		
	$\bar{X}$	4.69	6.15		
1 semana	D. E.	1.58	3.21	1.366	0.10 - 0.05
	F	1.53 - 7.85	0 - 12.57		
	$\bar{X}$	5.44	5.13		
1 mes	D. E.	3.09	1.97	.269	0.40 - 0.35
	F	0 - 11.62	1.19 - 9.07		

$\bar{X}$ = *Media aritmética*
D.E. = *Desviación estándar*
F. = *Fluctuación ("Range.") = media ± 2 D. E.*
* = *Significativo (0.05)*

ficativa entre sexos, a la vez que se observa una hipersecreción fisiológica de las hormonas tiroideas (1, 2).

A las muestras congeladas de 13 varones y 12 hembras del estudio de función tiroidea en infantes, le realizamos determinaciones de los niveles de hormona tirotropa, para elucidar si existía o no una hipersecreción de TSH en el período perinatal.

A modo de estudio preliminar, analizamos los niveles de TSH desde el primer día hasta los 6 meses de edad en un recién nacido varón y otro hembra. Ello nos mostró una hipersecreción de la hormona, en ambos, durante las primeras 72 horas, disminuyendo a la semana hasta los niveles aceptados como normales en los adultos (0-10 mU.I/ml). Por ello, acortamos el estudio en el resto de los sujetos hasta la muestra de un mes de edad.

Nuestro estudio, al igual que lo sugerido por los estudios de Fisher y Odell (4) y de Czernichov y colaboradores (5), demuestra que existe una hipersecreción fisiológica de TSH en los primeros días de

TABLA III
SECRECION DE TSH EN LAS PRIMERAS 24 HORAS

EDAD			
(<)´ Menor de 12 hrs.		(>) Mayor de 12 hrs.	
♂ n=9	♀ n=9	♂ n=4	♀ n=3
$\bar{X}$ 44.05	25.28	18.44	16.33
D. E. 18.87	10.45	13.96	11.12
F 6.31-81.79	4.38-46.18	0.-46.36	0.-38.57

vida. A diferencia de los estudios citados (4, 5), observamos que dicha hipersecreción persiste hasta las 72 horas de edad. El valor promedio (media aritmética, $\bar{X}$) de TSH circulante alcanza un máximo en las primeras 12 horas en ambos sexos y disminuye progresivamente en las primeras 72 horas, manteniéndose la fluctuación, en este período de tiempo, en niveles elevados comparados con lo normal del adulto.

La hipersecreción de TSH tiene lugar en las primeras horas de vida, secundaria probablemente al stress del parto, además del efecto del frío al nacer como han sugerido Fisher y Oddie (4). Estos autores han demostrado que la hiperactividad tiroidea del recién nacido es menor, si éste se protege del frío desde el momento del nacimiento.

Recientemente Hedge y Thompson (7) en Tucson, Arizona, han demostrado en ratas que las prostaglandinas pituitáricas endógenas influencian la secreción de TSH potenciando el efecto de la hormona descargadora de tirotrofina (TRH) hipotalámica. Esto nos hace pensar que en el momento del parto cuando indudablemente hay un incremento en los niveles de prostaglandinas, estos están contribuyendo a la hiperfunción tiroidea al facilitar la acción de la TRH sobre la pituitaria, dando lugar a hipersecreción de TSH. Ello es una mera suposición nuestra y nos sugiere la importancia de medir niveles de prostaglandinas en estos mismos sujetos para definir sus niveles y el curso que siguen éstos.

La diferencia existente en la secreción de TSH en las primeras 24 horas de vida entre los varones y las hembras es un hecho paradójico para el cual no encontramos explicación convincente alguna. Las hembras, sin embargo, paradójicamente, presentan niveles superiores de tiroxina total e índice de tiroxina libre (1, 2), e inferiores de captación de triiodotironina en resina, que los varones. Ello se ha atribuído al efecto estrogénico a partir de las hormonas maternas, el cual, por razón desconocida, es más manifiesto en hembras que en los varones. Aparentemente existen otras variables entre los sexos que dan lugar a estas diferencias, y que al momento desconocemos.

Resumen

Se estudiaron tos niveles circulantes de hormona tirotropa mediante técnicas de radioinmunoensayo en recién nacidos normales hasta el mes de edad. Se establecen los niveles normales para el método empleado, en esta edad.

Se establece que existe una hipersecreción de hormona tirotropa durante las primeras 72 horas de vida, la cual es más marcada en las primeras 12 horas, la cual daría lugar al estado de hipertiroidismo fisiológico que presentan los recién nacidos normales en la primera semana de vida. Se observa una mayor secreción de TSH en los varones que las hembras, siendo esta diferencia estadísticamente significativa en las primeras 24 horas de edad. Representa este el primer estudio longitudinal de niveles de hormona tirotropa circulantes en el período perinatal.

Summary

Normal TSH levels in a normal newborn population up to one month of age are established. Radioimmunoassay for TSH levels were performed on the blood samples of 13 males and 12 females, longitudinally, at age 0-24 hrs., 48-72 hrs., 1 week and 1 month.

Hypersecretion of TSH during the first 72 hours of life is demonstrated. The highest levels are observed during the first day of life, mainly in the first

12 hours, and most marked in males. Sex difference is statistically significant in the first 24 hours of life. Paradoxically, females have highest T-4 and free thyroxine index levels (as demonstrated in a previous study) than males. Apparently there exists some unknown mechanism to explain this sex difference. The probable relationship of maternal estrogenic effect, the effect of cooling, and the effect of stress and prostaglandins are included in the discussion.

Agradecimiento

Agradecemos a la Sra. Ive Lang de Ferriol, M.T., y al Sr. Rafael García, M.T. la ayuda técnica aportada, y a la Sra. Mirna Nazario la excelente labor secretarial.

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ANOMALOUS ORIGIN OF LEFT CORONARY ARTERY FROM PULMONARY ARTERY: REPORT OF A CASE ASSOCIATED WITH AN ATRIAL SEPTAL DEFECT

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Aberrant origin of the left coronary artery from the pulmonary trunk is an infrequent congenital malformation (1-90). This lesion was first described in a 5 1/2 months old infant by Abrikossoff in 1911 (3). Abbott had previously described the malformation in an adult in 1908 (2). Since then further cases were reported on a necropsy basis only. Clinicians have been able to recognize this abnormality during life after the classical and electrocardiographic description of Bland, White and Garland in 1933 (4).

Anomalous origin of the left coronary artery from the pulmonary trunk usually occurs as a single lesion. As such, it is characterized by a typical clinical, electrocardiographic and radiographic pattern. Very few reports are available in the literature that mention its association with other major lesions (10, 19, 20, 26, 31, 72, 73, 80, 84). The purpose of this paper is to report a case associated to an ostium secundum atrial septal defect.

Case Report

M. B. P. a 6 year old girl was admitted to Ponce District General Hospital for cardiac catheterization and surgery. On her first visit to the out-patient clinic, at the age of 2 1/2 months, the mother offered a history of frequent respiratory infections, occasional episodes of cyanosis, without loss of consciousness, and recurrent colicky abdominal pains. This pain provoked intense crying, pallor, coldness and sweating. Since this visit, the patient underwent several hospitalizations for treatment of congestive heart failure with occasional episodes of pulmonary edema.

Results of physical examination, on her last admission, showed an acyanotic 6 year old girl weighing 38 pounds with a respiratory rate of 24 per minute, a regular heart rate of 100 per minute and a normal body temperature. The blood pressure was 90/60 mm Hg at the upper extremities and 120/70 mm Hg at the lower ones. The peripheral pulses were full and present in all four extremities. The liver edge was felt 5 centimeters below the right costal margin. Dermatoglyphics were normal.

The precordial region was bulging. The apex was felt at the 5th intercostal space lateral to the left midclavicular line and felt hyperactive. The first heart sound was single and slightly accentuated at the apex. The second heart sound at the pulmonary area was single and markedly increased in intensity. There was a grade 3/6 high frequency long midsystolic ejection heart murmur along the left sternal border which was more prominent at the mid and upper left sternal border and radiated to the apex and back. A grade 1-2/6 low frequency mid-diastolic rumble that increased with mild activity was heard at the apex.

The Chest X rays (Fig. 1) showed marked cardiomegaly with a narrow upper mediastinum. The right heart border was prominent with a faint suggestion of a double shadow about one inch inside the right cardiac border. The main pulmonary artery and left atrial appendage segment of the left cardiac border bulged moderately. The apex was displaced down and laterally. The pulmonary vascularity was diffusely increased.

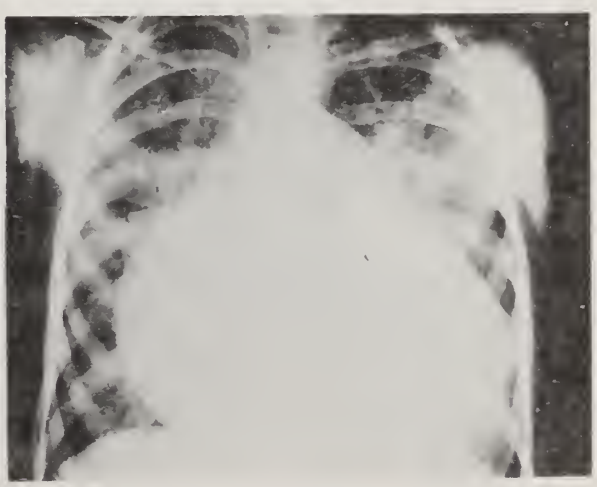


Figure 1

From the Ponce District General Hospital, Ponce, Puerto Rico.

The electrocardiogram (Fig. 2) revealed right deviation of the QRS axis, first degree atrioventricular block, right atrial enlargement and left ventricular hypertrophy with strain and/or digitalis effect pattern. The abnormal R/S progression from right to left precordial leads together with deep Q waves and ST-T wave changes over the left precordium suggested a myocardial infarct.

During the cardiac catheterization, the catheter was advanced from the right atrium to the right ventricle and pulmonary artery and across an interatrial communication to the left atrium and ventricle. The study revealed a marked increase in oxygen saturation at the right atrium without further significant increase at the right ventricle or pulmonary artery (Table I). Contrast material was injected into the left atrial cavity with immediate passage and opacification of the right and left heart chambers. Hemodilution of dye impeded visualization of the origin of both coronary arteries. The ventricular cavity looked dilated and the free wall moved pathologically. Following angiocardiography the child became distressed with sustained ventricular tachycardia and chest pain. Medical treatment was administered and the procedure ended.

Shortly after, the patient underwent open-heart surgery under cardiopulmonary bypass. A huge ostium secundum atrial septal defect was detected, together with an associated aberrant origin of the left coronary artery from the main pulmonary artery. Grossly, there was evidence of a poor collateral formation with an accompanying large left ventricular antero-lateral myocardial infarct. The surgical correction included patching of the atrial septal defect and ligation of the anomalous left coronary artery at its origin from the main pulmonary artery. The child expired during the immediate post-operative period despite resuscitative effort.

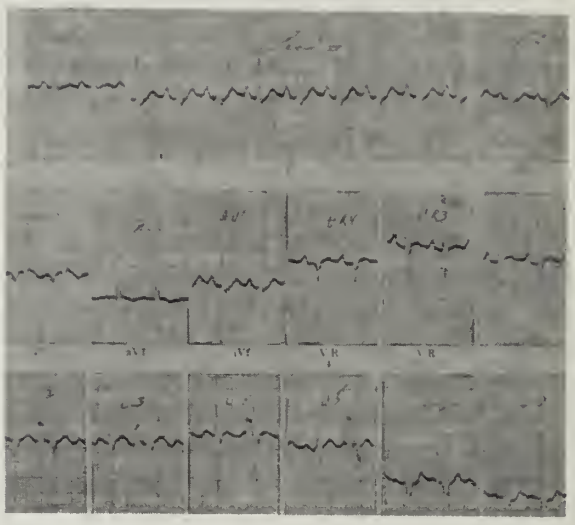


Figure 2

Discussion

Aberrant origin of the left coronary artery from the main pulmonary artery occurs infrequently. The incidence is approximately 0.24-0.48 percent among patients with congenital heart disease (87-90) and slightly more common in females than males (7, 89). It is believed to occur close to the end of the sixth week of embryonic life (89). Intercoronary anasto-

TABLE I
CARDIAC CATHETERIZATION DATA

Sample Site	O_2 Saturation (Percent)	Pressure (mm Hg)
Superior Vena Cava	57	
Right Atrium	88	11 (mean)
Inferior Vena Cava	79	
Right Ventricle	90	65/0/10
Pulmonary Artery	87	45/23
Left Atrium	95	10 (mean)
Left Ventricle	95	90/0/11
Aorta	95	90/60

moses are present normally during prenatal life (87-89).

Similarity of aortic and pulmonic oxygen content and arterial pressure, before birth, guarantees an adequate flow through the left coronary artery. The normal descent of pulmonic arterial pressure after birth endangers left ventricular myocardial perfusion. An adequate coronary perfusion depends then on the presence of large intercoronary anastomoses and on reversal of flow from the right coronary artery, through intercoronary collaterals, to the left coronary artery and finally into the pulmonary trunk (1, 21, 29, 30, 32, 39, 42, 45, 47, 50).

These circulatory adjustments have led to several classifications. Gouley (11), Agustsson and collaborators (36), and Gasul and co-workers (87) divided patients into infantile and adult types according to the presence of inadequate or adequate intercoronary communications respectively. Hemodynamically, a classification into 3 stages has been proposed by Nadas (47), Edwards (50) and Talner (52). The first stage includes the fetal and neonatal period when flow through the left coronary artery is antegrade from the pulmonary artery. The second stage comprises the period when left ventricular myocardial perfusion becomes inadequate giving rise to anginal pain and anterolateral myocardial infarct development. The last stage is represented by the onset of retrograde flow from the right coronary artery, through intercoronary anastomoses, and towards the pulmonary artery. Recently Baue (58) and Wright (71) have emphasized an additional stage when the left-to-right shunt becomes so copious that gives origin to a coronary artery steal syndrome.

Our patient presented in early infancy the classical picture of tachypnea, repeated respiratory infections, transient cyanosis, crying as if in pain with pallor, coldness and sweating that has been described by other authors (4-16, 19, 20, 24-28, 35-42, 46-48, 52-54, 63).

Usually patients do not have a murmur in early infancy or they may have a short systolic ejection unimpressive murmur (10, 23, 36, 40, 41, 48, 52, 55). There are several reports of the presence of a pansystolic apical murmur compatible with mitral regurgitation and explained on the basis of left ventricular posterior papillary muscle infarction and subsequent diffuse endomyocardial fibrosis (21, 27, 35, 37, 46, 48, 52, 53, 68, 70, 71, 81). Other investigators have described either a continuous or a systolic and diastolic murmur (20, 28, 36. 38, 39, 41, 44, 51, 55, 67). Turbulence through intercoronary collaterals or across the ostium of the aberrant left coronary artery has been given as an explanation to this murmur. The murmurs present in our patient may have originated at the tricuspid and pulmonary valves secondary to increased blood flow across them, however collateral flow although grossly inapparent may have contributed also.

The radiographic studies in anomalous origin of the left coronary artery usually reveal cardiomegaly with normal pulmonary arterial vascularity in the absence of acute pulmonary edema. The increment in pulmonary vascularity in our patient may have been a combination of augmented pulmonary flow secondary to the large left to right shunt at the atrial level and pulmonary venous hypertension secondary to left ventricular failure.

Several disease entities give rise to myocardial infarction in infancy (31, 88, 89), however the most common one is aberrant origin of the left coronary artery from the main pulmonary artery. These patients usually develop an anterolateral myocardial infarct characterized by wide and deep Q waves in leads I, AVL and V 5-7 together with ST-T wave changes in the same leads. This same pattern may be present in other rare lesions that should be excluded by angiocardiography (74, 77, 79, 83, 89). The QRS axis usually ranges from minus 60 degrees to plus 90 degrees (88). Our patient showed right deviation of the QRS axis together with a pattern of myocardial infarct on the precordial leads and left ventricular hypertrophy.

Heart catheterization may reveal a left-to-right shunt at pulmonary artery level, but more often than not, it is inapparent by oximetry. When oximetry fails to detect a shunt, the use of indicator dye, hydrogen electrode or fiberoptic catheter may bring out evidence of it at the pulmonary trunk level. The definitive study for an accurate identification of this lesion is selective supravalvar aortography (22, 29, 30, 39, 42, 45, 47, 49, 51).

There is an extensive bibliography on management and surgical treatment of this condition but only two operations remain as logical along the years (17, 18, 21, 23, 31-34, 36, 43-45, 55-67, 69, 71, 72, 75, 78, 82, 85, 86, 89). Advocates of ligation of the left coronary artery at its origin from the pulmonary trunk pursue an increase in myocardial perfusion in patients with an adequate intracoronary left-to-right shunt through an increase in intracoronary pressure. Other investiga-

tors are in favor of establishing a two coronary artery system by transplantation of the left coronary artery to the aorta that, when feasible, seems to be the most advantageous procedure.

Aberrant origin of the left coronary artery from the pulmonary trunk usually occurs as an isolated malformation. Very few reports deal with its association with other congenital cardiac defects. Lesions such as persistent patent foramen ovale (19, 31), ventricular septal defect (31, 73), persistent ductus arteriosus (10, 20, 26, 31, 72, 84), aortopulmonary septal defect (73), bicuspid right atrioventricular valve (72), pulmonic stenosis secondary to bicuspid pulmonary valve (84), angioma of the mitral valve (31), narrow aorta (26) and right aortic arch (73) have been mentioned in a casual manner. Association with an atrial septal defect has been informed twice before. The first case, a patient reported by Sabiston and coauthors, was a necropsy finding (31). The second report, by Arnott and collaborators, described a patient who underwent surgical correction of an ostium secundum atrial septal defect and mitral valve replacement. Only at autopsy was the presence of an aberrant origin of the left coronary artery from the main pulmonary artery recognized (80). Our patient represents the only case recognized in life with such a combination of congenital cardiac lesions.

Summary

Anomalous origin of the left coronary artery from the main pulmonary artery is an infrequent congenital cardiac defect. It usually occurs as an isolated lesion. A patient presenting this anomaly, in combination with an atrial septal defect, is reported. A review of the literature revealed two additional cases. Our patient represents the first case where recognition of the association of both lesions was made in life.

Resumen

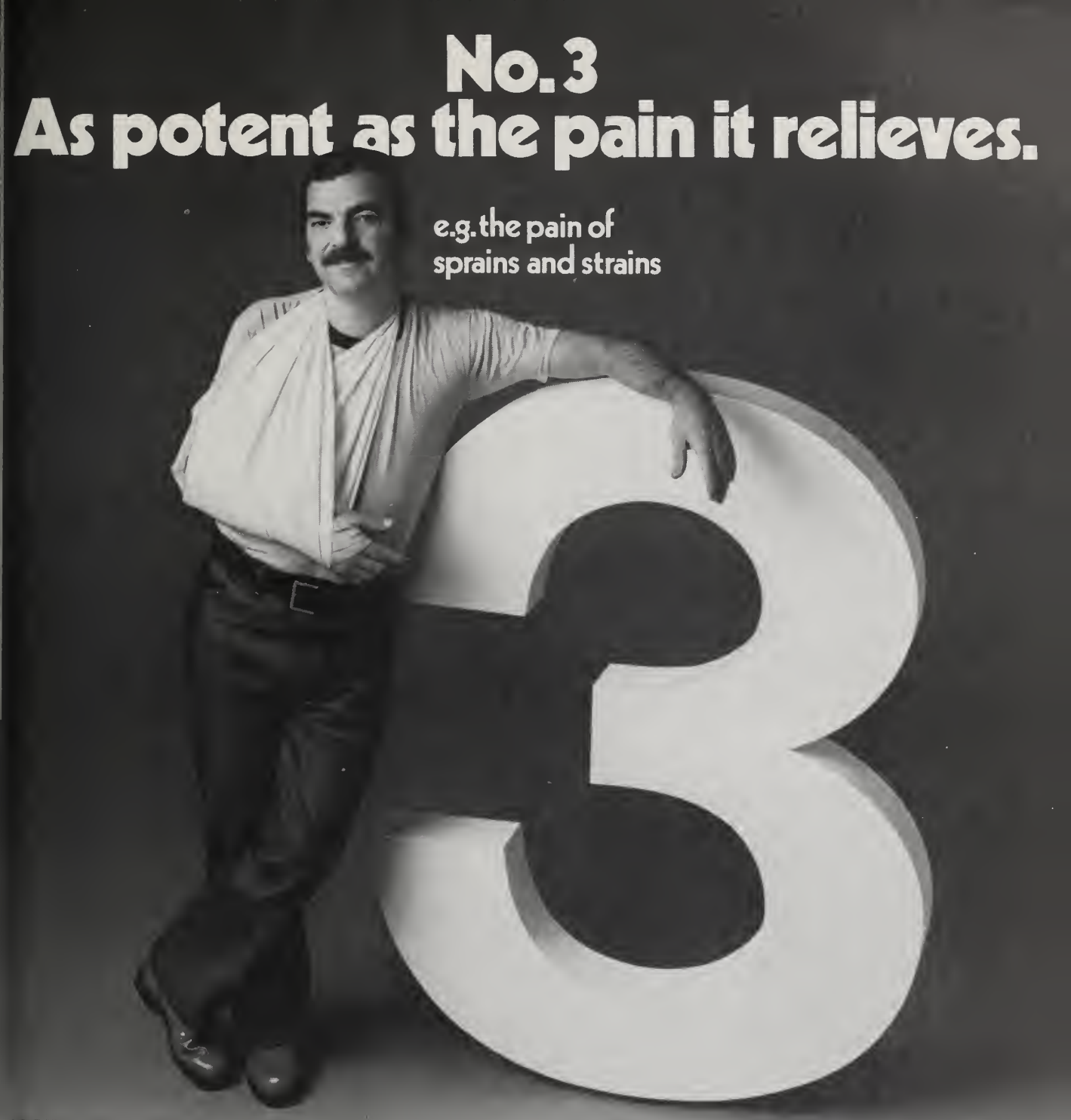
El nacimiento de la arteria coronaria izquierda del tronco de la arteria pulmonar es uan malformación infrecuente. Generalmente esta anomalía no va acompañada de otras lesiones. El presente informe muestra este defecto asociado a una comunicación interauricular. Repasando la literatura encontramos que nuestro caso es el único donde esta combinación fue reconocida en vida, constituyendo además el tercer ejemplo con dicha combinación de lesiones cardíacas.

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Sleep Stages

- Awake
- REM
- Stage 1
- Stage 2
- Stage 3
- Stage 4



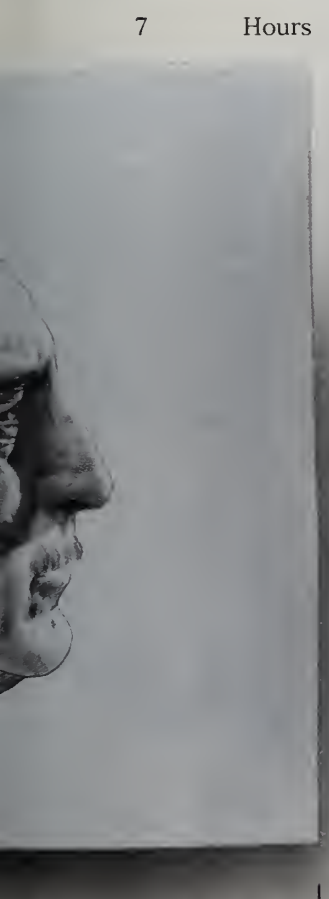
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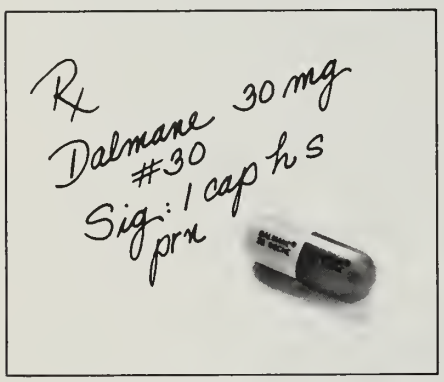
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Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

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SOME CLINICAL FEATURES OF VULVOVAGINAL MELANOMAS WITH CASE REPORTS

E. Pantoja, MD
F. E. Colón, MD
I. Rodríguez Ibañez, MD

For years surgeons have mastered the techniques required to handle the operable vulvovaginal melanomas, yet less than half of these patients are being cured (1), and early detection remains as the only hope of improving the surgical results. Early detection presupposes, in addition to public awareness and cooperation, a high index of suspicion coupled with a clinical knowledge of the disease on the part of the physician. To this end, the pertinent literature has been reviewed in conjunction with the analysis of our small series of cases. These cases have been summarized in the accompanying table.

Incidence

The vulva is by far the most common location of this tumor in the female genital organs. In fact, because of its size, the skin is, inch for inch, less frequent a site of melanoma than the vulva (2). Six to eight percent of all melanomas in the female occur in this site (3, 4), but compared to other vulvar lesions, malignant melanomas are less common, only one to three percent of all vulvar malignancies (1, 3, 4). Melanomas in the vagina are rare; in the cervix they are almost unheard of.

Induction of Malignant Melanoma

Most cutaneous nevi in the adult are innocent, being purely intradermal and having no traceable connection to the epidermis. In the female genitalia, they are generally associated with the so-called junctional activity (5); peculiar clear cells (melanoblasts) are seen infiltrating the various layers of the epidermis from their origin at the dermoepidermal junction (basal cell layer). The induction of malignancy is preceded by proliferation and anaplastic change in the melanoblasts while still confined to the epidermis, constituting essentially a melanoma in situ. When invasion of the dermis occurs, the lesion is a full fledged malignant melanoma (5). This early lesion may spread very superficially for a while, and if well pigmented, it will appear as a deceptively innocent dark brown or black discoloration (Fig. 1).

In the mucous membrane of the female genitalia nearly half of the melanomas are amelanotic (5) and some of the superficial non-pigmented lesions may be confused with extramammary Paget's disease, a confusion which is reinforced by the histologic similarity between Paget's cells and the clear cell melanoblasts. Allen has referred to this superficial non-pigmented lesion as the Pagetoid form of malignant melanoma.

Clinical Manifestations

The premalignant junctional nevus in the female genitalia is generally asymptomatic and attracts little attention even during the active phase of intraepidermal proliferation (3). Thus, the assertion of Goforth (6) that vulvar melanoma is a preventable disease (by removing vulvar nevi prophylactically, preferably before puberty) is somewhat over optimistic. Often the lesion is not discovered until it presents as a more or less pigmented mass (7) which may or may not be ulcerated (8). It is usually soft, fleshy and quite vascular. In the vulva it may be flat, nodular, or even pedunculated. The vaginal melanoma may be small and easily overlooked (9), or it may grow to occupy the whole space from the hymen to the cervix (8).

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TABLE
SIX CASES OF VULVO-VAGINAL MELANOMA

Case No.	1	2	3	4	5	6
Age	41	72	56	36	88	68
Parity	G 1, P 1	G 11, P 9, Ab 2	G 3, P 2, Ab 1	G 2, P 2	G 5, P 5	G 9, P 7, Ab 2
Histology	MM	MM	MM	Amelanotic MM	Amelanotic MM	MM
Site	R labium majus	Labia minora	R labium minus	Vagina	Cx & vagina	Urethra & vulva
Gross Features	Pigm vulvar lesion	Pigm lesion labia minora	Pigm lesion labium minus	Mass in upper 1/3 of vagina	Huge mass in Cx & Vagina	Periurethral pigm growth
Symptoms	Vulvar lesion	Vaginal bleeding	Vulvar lesion	Vaginal bleeding	Vaginal bleeding & back pain	Dysuria & Vaginal bleeding
Duration	2 mo.	2 mo	4 mo	3 mo	7 mo	6 mo
Treatment	No curative treatment	Local excision, vulvectomy & bil IN dissection 3 mo later for rec.	Local excision & superficial R groin dissection	Hysterectomy & subtotal vaginectomy. Radiation for rec later.	4500r pelvic radiation, repeated for rec tumor 6 mo later.	Partial urethrectomy & vulvovaginectomy
Survival in mo.	14	20	10	24	27	No rec. 12 mo post-surgery
Local rec	----	Rec 2 mo after local excision	No local rec after excision	Vag rec 8 mo post-surgery	Never controlled	None yet
Regional Metast.	Satellite skin lesions & bil. IN developed quickly.	IN neg at surgery, involved later.	Pos RIN at surgery, massive pelvic discase preterminally.	Vaginal rec followed by a L, then a R pelvic mass.	R parametrial infiltration & IN on admission	None
Systemic Metast.	Lung metastases within two mo of diagnosis	Bone & lung terminally	no	no	no	no
Remarks	Rapid systemic spread precluded curative treatment	Local spread after local excision, not controlled by late surgery.	Death from pelvic rec, no vulvar rec or systemic metast.	Death from pelvic tumor, ureteral obstruction & uremia.	Confused with Cx cancer, Stage III clinically.	MM of urethral meatus invading vulva. Free of tumor 12 mo post-surgery

MM - malignant melanoma, R - right, L- left, Rec - recurrence, IN - inguinal nodes, pigm - pigmented.

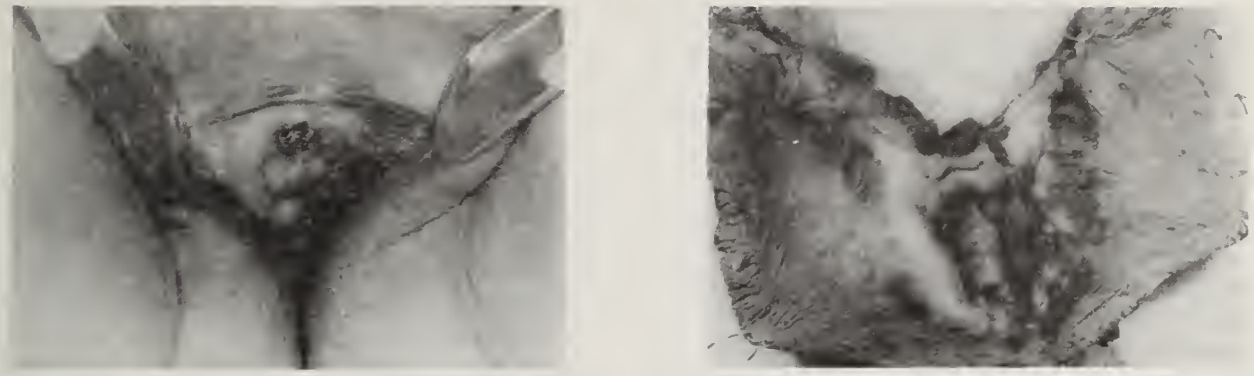


Fig. 1: *(A) Case 6. Preoperative photograph of a malignant melanoma of the vulva, periurethral type. Note pigmented extension of the tumor into the left labia. (B) Partially fixed operative specimen. The urethral canal has been opened from above. Note pigmentation of left labia.*



Fig. 2: *Case 4. Radiograph of the pelvis with contrast dye in the bladder showing pressure defects on both sides of this viscus due to pelvic tumors.*

The presenting symptoms depend on the location of the tumor. In the vulva it is likely to be the tumor itself, associated with more or less local discomfort. This is later followed by bleeding and discharge when ulceration develops. In the vagina, however, these symptoms are likely to be the first to attract attention to the disease (10). The bleeding may be slight, often only spotting; and if the patient is premenopausal, it may occur between cycles. It may show as post-coital bleeding (8, 11), associated sometimes with dyspareunia (8, 11) and frequently with a vaginal discharge. Thus, the presenting manifestations may suggest cervical carcinoma. Like the latter lesion, melanoma of the vagina may invade the parametrium, rectum, or bladder (8). Intrapelvic extension may produce a mass which compresses and distorts the bladder (Fig. 2), ureters (Case 4), or rectum. The disease may also involve both cervix and vagina causing difficulty in identifying the site of origin, and sometimes even closely resembling carcinoma of the cervix, as Case 5 clearly illustrates.

This patient was admitted to a cancer hospital where the gynecology staff is thoroughly familiar with cervical cancer, this being the most frequent malignancy among Puertorrican females. Yet, not only was the true nature of her disease misinterpreted on the initial examination, the impression being that it was cervical carcinoma, stage III, but when the biopsy revealed a malignant melanoma the patient was re-examined in disbelief, and it was now suspected that the two lesions surely coexisted. Multiple biopsies, however, consistently revealed malignant melanoma.

A similar case of melanoma involving both the cervix and the vagina was reported by Taylor and Tuttle (12). In their case the tumor bled so heavily following the biopsy that a vaginal hysterectomy had to be performed to control the hemorrhage. This is an unusual occurrence despite the fact that these tumors are quite

vascular and that bleeding has often been reported as the most important symptom (10, 13). The case of Taylor and Tuttle lived for thirteen years with local but progressive disease, and towards the end she experienced another unusual symptom of this illness, melanuria.

Melanuria and melanosis are very rare manifestations of this tumor which have occasionally been reported in genital melanomas (12, 14). The excretion of large quantities of melanin in the urine or deposition of the pigment in the tissues depend on the balance between production and the various means of disposing of this substance in the body. Normally melanin is lost through the skin by way of epidermal attrition, through phagocytosis, and urinary excretion. The total quantity of melanin in an individual is normally small; the entire skin of a black man is said to contain only about one gram of this pigment (15). On the other hand, up to three hundred grams of it have been recovered from a malignant melanoma (15). Obviously, the development of melanuria and melanosis must be related to the bulk of the tumor and to its capacity to form melanin.

When pigment formation is abundant, the diagnosis of vulvovaginal melanomas may be suspected on pelvic examination, the appearance being quite characteristic (Fig. 1). Similarly, the cutaneous metastases of a primary vulvar melanoma may be pigmented and easily recognized (16). However, when the lesion is amelanotic, as our cases 4 and 5, the diagnosis must depend on adequate histologic studies. Such entities as extramammary Paget's disease, Bowen's disease, and epidermoid carcinoma must be distinguished from amelanotic melanoma of the vulva. A biopsy is indispensable in all cases to establish the correct diagnosis.

Summary

Six cases of vulvovaginal melanoma were studied. Four of these occurred in the vulva, one of which was periurethral in location. The other two involved the vagina; these were both amelanotic and one invaded the cervix too. The latter was clinically confused with carcinoma of the cervix, the symptoms of which may be imitated by vaginal melanomas. Other clinical features of vulvovaginal melanoma are reviewed.

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The explosion in knowledge and information in medicine has made it difficult for the busy physician to keep up with the medical literature, even within the limited field of his own particular interest. This section is presented in an effort to bring you reviews of subjects that may be important. It is hoped that the reader will be stimulated to pursue the reading further and to come up with criticisms or suggestions.

Three articles dealing with the terminal ileum have been selected for review. The wide ranging implications of pure and applied knowledge of this interesting segment of the gut needs emphasis and is thereby presented.

Orlando Salichs, MD

TREATMENT OF CHOLERHEIC DIARRHEA WITH HYDROPHILLIC COLLOID

Disease of the Colon and Rectum, May 1975, by W. Grant Thompson, is reviewed. Eight patients with ileal resection diarrhea being treated with cholestyramine were then changed to hydrophillic colloid. Both drugs reduced overall frequency and improved consistency. It appears that cholestyramine * was effective at a lower dose than hydrophillic colloid **.

COMMENT: More and more interest is being shown in the ileum physiology and certainly after obligatory resections in right hemicolectomy, resection for granulomatous diseases or vascular catastrophies in neonates makes it mandatory for abdominal surgeons to be conversant with the implications of resections of distal ileum and ileocecal valve. There seems to be a quantitative relationship as to length of ileum resected to production of diarrhea; effects in bile acid pool with its relationship to gallstone formations; or in colonization of small intestinal flora in those patients that the ileocecal valve is sacrified. The next two articles will deal with the latter two problems.

* - *Cholestyramine (Questran or Cuemid)*
** - *Hydrophillic Colloid (Metamucil)*

CHOLELITHIASIS AND ILEAL PATHOLOGY IN CHILDHOOD

Cholelithiasis and Ileal Pathology in Childhood by D. Pillerin, P. Bertin, Cl. Nihoul-Fekete and Cl. Ricours in the Journal of Pediatric Surgery, February, 1975 is reviewed.

The usual cause of gallstones in children is congenital hemolytic jaundice. The authors review their experience with 18 patients (children), four of whom developed stones after resection of the small intestine. One was an eight month baby with necrotizing enterocolitis requiring resection of jejunoileum with 80cm. of small intestine preserved. Seven months later X-rays revealed gallstones. The second case required 50cm. ileal resection for ileal atresia and volvulus. A gallstone was demonstrated by X-ray, at 20 months of age. The third case was of a nine month old infant requiring resection of a small intestine segment with end to end anasto-

mosis for cystic lymphangioma of intestine and the fourth case, age five, was of one of Wilms' tumor, who was given irradiation after nephrectomy, chemotherapy and who required resection of a segment of small intestine, seven months later for radiation strictures. He developed gallstones two years later. All four cases required cholecystectomy.

COMMENT: The role of the terminal small intestine in the metabolism of bile via the enterohepatic cycle is of pivotal importance. The formation of gallstones, following ileal resection is of clinical importance. Bile salts are synthesized by the liver and conjugated with tauri and glycocollic acids and as cholates form a micellar solution keeping cholesterol and lecithin soluble (see Small triangular coordinate concept). Then they are secreted into the duodenal lumen, the bile salts being necessary for the absorption of fats. The bile salts are actively reabsorbed in the distal ileum and passively reabsorbed in the rest of the small intestine, being returned to the liver via the portal vein, making 6-8 cycles a day with an average pool of 290mgm/m2, with obligatory minimal fecal loss made up by fresh synthesis by the liver. Resection of the ileum or impairment due to ileitis interferes with this enterohepatic cycle and even with increased liver synthesis to compensate for the augmented fecal loss, the bile salt pool is diminished and leads to malabsorption of fats (use of this is made in ileal exclusion to reduce cholesterol, hyperlipemia and obesity). Bile becomes lithogenic with oversaturation of cholesterol as a result of ileal resection and interference of the concentrations of cholesterol, lecithin and bile salts, with ensuing cholelithiasis.

THE SIGNIFICANCE OF THE ILEOCECAL VALVE IN MASSIVE RESECTION OF THE GUT IN PUPPIES

The Significance of the Ileocecal Valve in Massive Resection of the Gut in Puppies by Ian S. Reid in the Journal of Pediatric Surgery of August, 1975 is reviewed.

The preservation of the ileocecal valve is vital to survival in newborn infants with near total loss of the small bowel. As a rule, babies with less than 40cms of remaining small intestine and no ileocecal valve are most unlikely to survive. Twenty-four puppies underwent 90 percent resection of the small bowel and twelve of these also had destruction of the ileocecal valve by a longitudinal incision and transverse repair. Of the 12 puppies with resection alone 8 survived and of the 12 puppies with resection and valvotomy only one survived. The one puppy surviving with valvotomy had a Z-shape kinking of the small bowel which was considered to be acting as a valve.

COMMENT: The function of the ileocecal valve as a barrier to bacterial contamination, from the colon and the resultant colonization of the ileum when the valve is destroyed is very pertinent. The dilemma of having to resect the lower ileum with the ileocecal valve is a real one, and every effort to preserve intact the ileocecal valve should be made especially in cases of vascular or necrotizing enteritis in children. The "second look" operation in cases of necrotizing enteritis or vascular intestinal catastrophe may be the best course of action, 8-12 hours later, in an effort to salvage the ileocecal valve and most distal ileum. If one has to resect small bowel it is far better to resect more intestine proximally and save more distally where active absorption processes and ileocecal valve competence seems crucial for survival and better quality of life.

LIQUID SILICONE USEFUL IN SMOOTHING FACIAL LINES

CHICAGO– Liquid silicone has been thoroughly discredited for use in enlarging breasts, but it still is a useful product in small amounts in smoothing out deep lines, wrinkles and sunken scars of the face, says a report in the September issue of Archives of Otolaryngology, a publication of the American Medical Association.

Legitimate cosmetic uses of liquid silicone have been slowed down greatly as a result of the widespread adverse publicity given to the product in breast augmentation, says Robert A. Berger, M. D., dermatologist of Mount Sinai School of Medicine, New York, N. Y.

If the silicone is injected properly and in the proper small amount, it does not shift under the skin, he reports. Damage to breasts came when large amounts, up to half a pint or more, were injected directly to make the breasts larger.

INTESTINAL PARASITE INFECTS TRAVELERS TO LENINGRAD

CHICAGO– On your next trip to Leningrad, don't drink the water. You might pick up giardiasis.

Giardia lamblia is an intestinal parasite that won't kill you but can make you very sick. It exists all over the world, but a recent report found that almost one-fourth of American tourists returning from the Soviet Union, and especially those who visited Leningrad, had picked up the bug.

Martin S. Wolfe, M. D., of the Tropical Medicine Unit of the Department of State, Washington, D. C., reports returning travelers with the stomach ailment in the September 29 issue of the Journal of the American Medical Association. The same issue also includes an editorial on giardiasis by Myron G. Schultz, M. D., of the Center for Disease Control, Atlanta, and another report by T. W. Sheehy, M. D., and D. Brandt, M. D., of Birmingham, Ala., on how the parasite can cause a malfunctioning pancreas by inducing malabsorption.

Many Americans pick up the disease at home, but many cases also are reported among returning travelers. Victims have diarrhea, weakness, weight loss, stomach cramps, nausea, excessive abdominal gas, vomiting, belching, and, sometimes, fever.

The symptoms of giardiasis mimic several other intestinal infections that tourists often contract, and diagnosis is difficult, requiring additional tests, says Dr. Wolfe. Once the diagnosis is established, then drugs are available that bring a very high cure rate. Or sometimes the infection will wear itself out without treatment, if symptoms are not too severe.

There's no drug you can take to prevent giardiasis. The same precautions apply as are listed for the other "turista" causes – avoid tap water unless it is boiled or treated with an iodine compound such as Globaline, avoid uncooked or unpeeled fruits and vegetables. But even with precautions some individuals will become ill.

Fortunately, giardiasis is not fatal. It works slowly, and the tourist on a short trip frequently is back home before the symptoms strike.

HOME AQUARIUMS MAY HARBOR INFECTION

CHICAGO– A nasty little bug sometimes lurks in your lovely home aquarium. If you should scratch your finger while cleaning the aquarium, you might develop a skin ailment known as Aquarium Granuloma.

In the September 29 issue of the Journal of the American Medical Association John J. Van Dyke, M. D., and Kevin B. Lake, M. D., of La Vina Hospital in Altadena, California, report on two women who developed infections from aquariums.

One patient got a scratch in cleaning her home aquarium. A sore developed on the thumb, then others on the forearm. They were opened and drained and once diagnosis was established, cured with drug treatments. The other patient worked in a pet shop, and cut her finger on an aquarium.

The offender is mycobacterium balnei. It already had been known as cause of skin infections in swimmers, but only recently has it been known that aquariums also may harbor the bug.

LIQUID SILICONE DANGEROUS FOR ENLARGING BREASTS

CHICAGO– Further evidence that liquid silicone for enlarging breasts is dangerous is reported in a fall issue of the Journal of The American Medical Association.

Three New York physicians report on several cases of serious illness and one death among individuals who had been given liquid silicone injections to enhance breasts. Two were transsexual men and the others were women. Granules of the silicone had migrated through the body and had entered the liver, with serious complications.

Richard Ellenbogen, M. D., of Stony Brook Medical School, East Meadow, N. Y., and colleagues reports that "adverse

systemic effects of silicone injections suggests that considerable ongoing clinical research is needed before release of this potentially lethal and debilitating substance into general clinical use."

The death occurred only ten hours after a woman received large injections of silicone under each breast. Silicone was found in the lungs, kidneys, liver, brain and blood.

GRANDSONS OF ALCOHOLICS RISK DRINKING PROBLEMS

CHICAGO– If grandpa was an alcoholic, watch your own drinking. Grandsons of alcoholics are three times as likely to have drinking problems as the general male population, says a report in the November issue of Archives of General Psychiatry, a publication of the American Medical Association.

By the time they were in their 50s, the grandsons of problem drinkers had become problem drinkers themselves at a rate of 43 percent, some three times that of the general male population, say two Swedish researchers from the University of Lund, Malmo, Sweden.

Actually, the study was set up to find whether some heredity factor causes excessive drinking in some men. Alcohol abuse is much more common among men than women. The researchers did not find a gene involved in transmitting a tendency to abuse drink, they say.

Sweden has kept records on problem drinkers for many years, and these files made possible the present study. The report is by Lennart Kaij, M. D., and Jan Dock.

RADIATION TREATMENT CONTROLS SOME TYPES OF BREAST CANCER

CHICAGO– Success in controlling some types of breast cancer by radiation treatment rather than surgery is reported by a Harvard Medical School team in the November 10 issue of the Journal of the American Medical Association.

M.D.s Erick Weber and Samuel Hellman report on treatment by radiation alone of one hundred women with localized breast cancer during a five-year period. Many of the patients were elderly and infirm and poor candidates for massive breast surgery, and a few were physicians' wives or younger women who firmly refused to have a breast removed.

In 40 of the patients, the small lump was removed by simple surgery. In others, treatment was by radiation alone. The radiation was applied externally, and also by small implanted devices that gave off continuing radiation in the immediate area of the cancer.

The physicians conclude that radiation therapy offers excellent local control in breast and chest wall cancers, with survival rates comparable to those treated by radical surgery. Radiation therapy should be considered for early breast cancer in women with strong emotional fears regarding the surgical deformity of breast removal, they declare. In more advanced cases, drug therapy can be combined with radiation therapy, they say. Ten percent of the patients treated experienced some complication from the X-ray therapy.

SCREENING PROGRAMS URGED TO DETECT THYROID PROBLEMS

CHICAGO– The American Medical Association and the American Hospital Association are conducting a joint campaign to encourage state and local medical and hospital societies to begin screening programs for persons who underwent radiation therapy of the neck and face during the 1930s through the 1950s.

Studies have shown that radiation therapy – commonly used until 20 years ago to shrink infected tonsils, adenoids and thymus glands in children – may be followed by a high rate of thyroid cancer and by other abnormalities of the thyroid gland.

Many hospitals and medical societies have started campaigns to find the thousands of former radiation therapy patients and screen them for thyroid cancer. The joint AMA-AHA recommendation encourages hospitals and physicians to work together to find potential cancer patients, through free screening programs, referral systems and publicity campaigns in the news media.

A recent letter to all state medical societies, signed by AMA executive Vice President James H. Sammons, M. D., and AHA President J. A. McMahon, described the best treatment for thyroid cancer – suppressive treatment rather than surgery in most cases – and summarized efforts in some areas to set up the screening programs. Programs have been developed in Cincinnati, Milwaukee and in Illinois, among others.

Thyroid cancer is a slow-growing cancer that rarely threatens life, so that conservative treatment is recommended by the AMA and AHA.

CHOKING MANEUVER ENDORSED BY AMA COMMISSION

CHICAGO– The Heimlich Maneuver – a life-saving first-aid technique to rescue individuals choking on food – receives the official endorsement of the American Medical Association's Commission on Emergency Medical Services in the Oct. 27 issue of the Journal of the American Medical Association.

"The Commission believes the maneuver to be a most important addition to the emergency care procedures for the person choking on food or other objects that shut off the airway," says the statement.

"Food chocking is the sixth leading cause of accidental death – victims number more than those accidentally killed

by firearms or in airplane accidents."

To perform the Heimlich maneuver—

Stand behind the victim (who is choking on food) and wrap your arms around his waist.

Grasp your fist with your other hand and place the thumb side of your fist against the victim's abdomen, slightly above the navel and below the rib cage.

Press your fist into the victim's abdomen with a quick upward thrust. Repeat several times if necessary, until the food is expelled.

Objects expelled by means of the maneuver include beef, chicken, lettuce, apples, popcorn, hot dog roll, mashed potatoes, pills, and candy. In six reports, the victim successfully self-administered the maneuver to relieve chocking.

In another article on the same issue, M.D.'s Robert Visintine and Choong H. Baich of Santa Ana, Calif., report on the case of a 74-year-old man whose stomach was ruptured by a companion in performing the Heimlich maneuver. The maneuver possibly could cause rupture of internal organs, but despite this risk the patient could owe his life to the prompt use of the technique in reopening his airway. In the one case reported, surgery corrected the internal damage and the patient recovered.

MEDICAL SCHOOL ABANDONS SHORTENED TRAINING PROGRAM

CHICAGO— Are medical schools becoming disillusioned with the effort of the past decade to shorten the training period for physicians?

At least one medical school has — Rush Medical College in Chicago — and is changing its training period from the abbreviated three-year course to four years.

In a report in the Oct. 27 issue of the Journal of the American Medical Association, William F. Hejna, M. D., Rush dean, says:

"Many of the arguments advanced in favor or shortening the standard medical school curriculum to three years may no longer be valid, and such shortening may cause tensions among students and faculty. Further, this innovation does not materially address issues such as physician availability, quality and maldistribution."

Dr. Hejna points out that — in response to the need for more physicians — in the past ten years some 50 schools have instituted regular or optional three-year curricula. In the late 1960s, he says, there was widespread attention to a national shortage of physicians.

As a result the number of schools has grown from 98 in 1968 to the present 114. Existing schools also increased enrollment, and there was a corresponding increase in first-year students from 9,000 to 15,000. This will very soon cause a significant increase in the number of physicians practicing in the United States. There also has been a sharp upswing in migration of physicians from other countries to the U. S.

Thus, the doctor shortage is rapidly being met, and is no longer a valid reason to maintain a three-year medical course, Dr. Hejna says. He points out that the body of fundamental biomedical science which the medical student must absorb continues to increase, and that the behavioral sciences have taken on new importance and time in medical schools.

At Rush, 55 percent of the students favored extending their training to four years. The shorter course meant going to school straight through the summer, with no break for three full years in the demanding study schedule.

DE LA COMISION PARA SEGURIDAD EN EL TRANSITO ELA NOS ENVIAN UN ARTICULO EXTRAIDO DEL BOLETIN "STATUS REPORT" EDITADO POR EL INSTITUTO PARA LA SEGURIDAD EN EL TRANSITO DE WASHINGTON, D. C. EL CUAL PUBLICAMOS A CONTINUACION YA QUE AMERITA PUBLICARSE POR SER DE INTERES PARA LA CLASE MEDICA:

SIMPLE TEST SHOWS ALCOHOL IN TRAUMA VICTIMS

A group of Maryland researchers has discovered that a simple emergency room procedure can provide an important aid in diagnosing the presence and amount of alcohol in trauma patients.

The study also revealed the presence of alcohol, in varying amounts, for 42 percent of the 565 emergency room patients studied.

The patients studied were all hospitalized during 1974. Routine serum osmolality tests, using what is called the freezing point depression method, were made. The study said that the method used in these tests proved "highly accurate.....inexpensive, and takes approximately two minutes to perform," and that the results correlate highly with blood alcohol concentrations.

The researchers pointed out that this "simple rapid estimate of blood alcohol concentration in the acutely injured patient has significant practical implications." They said, "It is well known that the smell of alcohol on the breath can lead to grave medical errors." Their test, on the other hand, could show whether the alcohol level was low — a sign that would caution the physician against attributing to alcohol physical signs such as a depression of consciousness — or high, thus reminding the physician of effects of alcohol he might otherwise not have considered in his diagnosis.

The researchers said they undertook the study because of the "perennial problem encountered by the emergency room physician or trauma surgeon" in interpreting "traditional clinical signs in an acutely traumatized patient with..... alcohol or drug ingestion." Since blood or serum alcohol tests are not readily available in most emergency rooms, the researchers looked at this simple test to see if it would

provide an accurate indication of alcohol.

"The importance of routine testing is suggested by the fact that almost half of our trauma admissions are positive for alcohol, and 64 percent of these have concentrations of 0.10 percent or higher, a level that constitutes presumptive evidence of intoxication in most states, and one which may complicate the diagnosis and management of trauma patients," the study said.

The research was supported by the Maryland Medical-Legal Foundation and the Insurance Institute for Highway Safety. "Alcohol Intoxication and Serum Osmolality" was published in The Lancet, June 28, 1975.

HEW NEWS:

The Department of Health, Education, and Welfare approved amendments to Social Security regulations providing for expedited appeals to the courts in cases where the only issue is the constitutionality of the law.

At present, a claimant is entitled to judicial review of a decision on a social security, Medicare, black lung, or supplemental security income claim if he has received an adverse initial determination and has exhausted his administrative appeal rights at the reconsideration and/or hearing and Appeals Council levels. Where appropriate, the new regulations will permit the parties to pursue an expedited judicial appeal after the claimant has received at least a reconsideration determination.

"Besides permitting the claimant speedier access to the courts, the expedited process will also conserve administrative resources," the Department noted. "If it is determined that a person's claim is appropriate under the expedited appeals process, an agreement will be drawn up specifying the facts in the case, the constitutional issue involved, and the decision to be reviewed. A determination denying the use of the expedited procedure will not be subject to the right to administrative or judicial review."

The regulations were promulgated in response to a Supreme Court decision in the case of Salfi vs. Weinberger. The court ruled that "it would be inconsistent with the congressional scheme to bar the Department from determining in particular cases that full exhaustion is not necessary for a decision to be 'final'..."

The amendments become effective with its publication in the Federal Register.

Health care spending in the United States reached $118.5 billion in fiscal 1975, with public spending increasing at almost twice the rate of the previous year.

A study, "National Health Expenditures," published by the Social Security Administration's Office of Research and Statistics, noted that the $118.5 billion health care bill represented a 13.9 percent increase over the $104 billion spent in fiscal 1974. This was the largest dollar increase in history, largely due to the removal of mandatory economic controls that were in effect in fiscal 1973 and most of fiscal 1974.

Public spending increased by 22.2 percent, compared with a 12.3 percent increase in 1974. This was more than two and one-half times the rate of increase in private spending for health care.

Public spending amounted to $49.9 billion, or 42.2 percent of the 1975 total, an increase of 22.2 percent, or $9.1 billion. Private spending—mainly private insurance and out-of-pocket payments—accounted for $68.6 billion, or 57.8 percent of the total health care expenditures for 1975. This portion was up 8.6 percent, or $5.4 billion, over 1974.

Other highlights of the research and statistics note:

—The acceleration in health spending in 1975 coupled with a slowed growth in the Gross National Product resulted in a significant increase in its share of the GNP—8.3 percent. Had the GNP increased at the 1974 rate, the proportion of health expenditures to GNP would have been about 8 percent. The fiscal 1975 increase came after a 3-year stable level of about 7.8 percent.

—Health spending averaged $547 per person, up from $484 per person in 1974. Direct out-of-pocket payments in 1975 amounted to $155 per person, compared with $146 the previous year.

—Hospital care continued to be the largest expenditure category, amounting to $46.6 billion, or 39 percent of the total spending. Physicians' services accounted for $22.1 billion, or 19 percent.

More detailed analysis of national health expenditures in fiscal 1975 will appear in the February issue of the Social Security Bulletin.

ANUNCIOS

SE VENDE O ALQUILA

Se vende, o se alquila, oficina Núm. 404, en las Americas Professional Center, al lado del Hospital del Maestro. Puede usted comunicarse con el doctor Rafael Méndez Cortés, teléfonos 766-3655, 723-8850, o 766-3179.

ATENCION MEDICOS

Se vende casa ideal para oficinas. Localizada en la calle Piñero Núm. 79, la calle donde está el nuevo centro de Diagnóstico de Río Piedras, cerca de laboratorios, rutas de guaguas, parking soterrado y a dos casas de la calle Núm. 1, donde pasa todo el tránsito hacia el centro del pueblo. (Tiene amplia marquesina caben cuatro autos).

El solar tiene 271 metros cuadrados, totalmente cercados. La casa es de dos (2) plantas, toda de hormigón armado. La planta baja tiene tres dormitorios, sala-comedor, cocina, cuarto de baño, balcón, terraza y marquesina, rejas en las ventanas, balcón y portones. Tiene screens en las ventanas y puertas.

La planta alta es de dos dormitorios y "Family-Room"-comedor, cocina y baño. Siempre está alquilada. Paga $233.00 mensuales, tiene hipoteca de $27,000.00.
"Opción" - $55,000.00

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Llamar de lunes a viernes después de las 6:00 p.m. Sábados y domingos todo el día, al teléfono 766-5952.

Tel. Oficina Sr. Alonso 783-3066
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ARTICULOS A PUBLICARSE EN LA EDICION DE FEBRERO

1. **Cáncer del Pulmón** - *Abel R. González, MD, Víctor Lister, MD y Jorge O. Just Viera, MD.*
2. **Assessment of Vitamin B_{12} Absorption in Tropical Sprue Utilizing Whole Body Counter** - *José J. Corcino, MD, René Dietrich, MD and Aldo E. Lanaro, M. D.*
3. **Diffuse Esophageal Spasm** - *José Ramírez Rivera, MD and Carlos Micames, MD.*
4. **Focal Nodular Hyperplasia of the Liver** - *Bernardo J. Marqués, MD and Queeland Morales, MD.*
5. **Trichophytobezoar of the Entire Small Intestine** - *Abelardo Alvarez, MD, María Castillo, MD, Reginald W. Freeman, MD, Haissy Noriega, MD and Eduardo de León, MD.*
6. **Foro de Medicina Nuclear** - *Carmen Caballero, MD y David Pérez, MD.*
7. **Editorial - Prognosis en el Cáncer Pulmonar** - *David Rodríguez Pérez, MD.*

Breast self-examination:

KEY ROLE OF THE PHYSICIAN

item:	**Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.**
item:	**Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, *fewer than 1 in 5* women practice BSE, and *only half* have an annual breast examination by a physician.**
item:	**Only 35% of all women polled reported that a *physician* had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.**
item:	***But,* among women who received personal instruction from their physicians, the overwhelming majority *(92%)* practiced BSE during the preceding year.**

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE.

The American Cancer Society gives major emphasis to breast cancer through research and a vast array of public educational materials, designed to give women life-saving information about the disease. Our latest approach is via a pioneering television film starring Jennifer O'Neill, "Breast Cancer: Where We Are." Where we *will* be in a few years will certainly hinge on our joint efforts.

American Cancer Society®

"Wynken, Blynken, and Nod one night Sailed off in a wooden shoe,-"

Colic, vomiting and other symptoms of milk intolerance needn't interfere with his sleep, if you've put him on NEO-MULL-SOY® formula. We've eliminated the common causes of feeding problems—milk protein and lactose intolerance, gluten sensitivity. And we're the first *corn-free* soy isolate formula. NEO-MULL-SOY is the whitest soy formula with milk-like appearance and consistency which appeal to mothers. It supports normal growth and development of the infant. And, it's kosher.



NEO-MULL-SOY®

Milk-Free Soy Isolate Formula
For the Milk-Intolerant Infant

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PALO ALTO, CALIFORNIA 94304

Ingredients per 100 grams of concentrate: water 75.2 g., sucrose 12.9 g., soy oil 6.9 g., soy protein isolate 4.0 g., potassium citrate 0.47 g., tricalcium phosphate 0.44 g., dibasic magnesium phosphate 0.11 g., lecithin 0.1 g., salt 0.06 g., calcium carrageenan 0.028 g., ascorbic acid 0.025 g., l-methionine 0.025 mg., choline chloride, ferrous sulfate, dl-alpha-tocopheryl acetate, niacinamide, zinc sulfate, manganese sulfate, d-calcium pantothenate, vitamin A palmitate, riboflavin, cupric sulfate, thiamine hydrochloride, pyridoxine hydrochloride, vitamin D_3, potassium iodide, folic acid, vitamin B_{12}.

APPROXIMATE ANALYSIS

	Undiluted	Diluted with an equal volume of water
Water	75.5%	87.8%
Protein	3.6%	1.8%
Fat	7.0%	3.5%
Carbohydrate	12.8%	6.4%
Minerals (Ash)	0.9%	0.5%
Calcium	0.17%	0.085%
Phosphorous	0.13%	0.06%
Iron	0.002%	0.001%
Calories per fl. oz.	40	20

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Chronic urinary tract infection



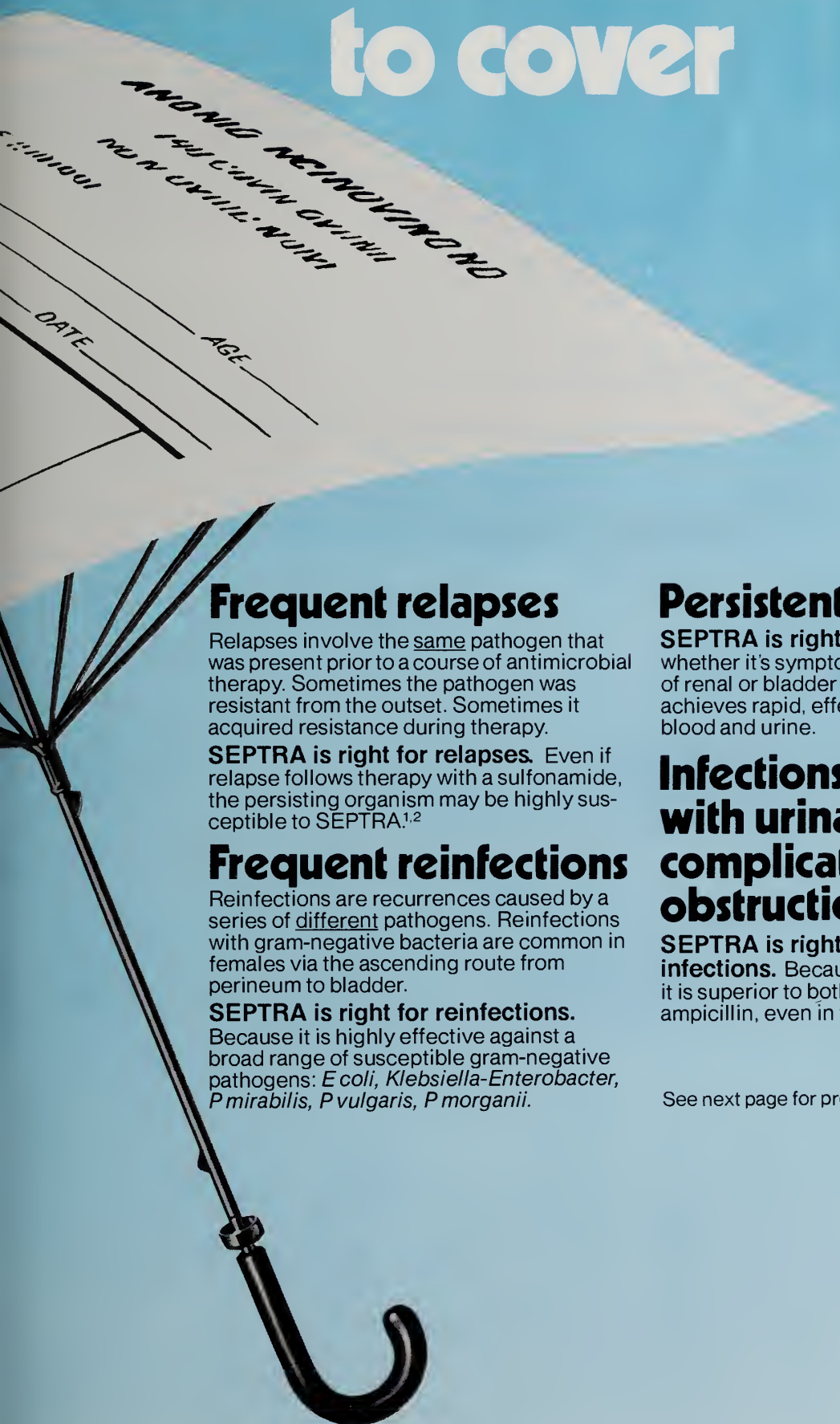
No matter how you define "chronic"

SEPTRA

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazole

A broad indication to cover



Frequent relapses

Relapses involve the same pathogen that was present prior to a course of antimicrobial therapy. Sometimes the pathogen was resistant from the outset. Sometimes it acquired resistance during therapy.

SEPTRA is right for relapses. Even if relapse follows therapy with a sulfonamide, the persisting organism may be highly susceptible to SEPTRA.[1,2]

Frequent reinfections

Reinfections are recurrences caused by a series of different pathogens. Reinfections with gram-negative bacteria are common in females via the ascending route from perineum to bladder.

SEPTRA is right for reinfections. Because it is highly effective against a broad range of susceptible gram-negative pathogens: *E coli, Klebsiella-Enterobacter, P mirabilis, P vulgaris, P morganii.*

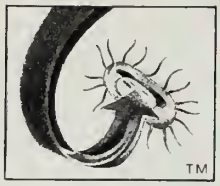
Persistent bacteriuria

SEPTRA is right for bacteriuria, whether it's symptomatic or asymptomatic, of renal or bladder origin. Because SEPTRA achieves rapid, effective levels in both blood and urine.

Infections associated with urinary tract complications, such as obstruction

SEPTRA is right for complicated infections. Because clinical studies indicate it is superior to both sulfamethoxazole and ampicillin, even in these difficult cases.[3]

See next page for prescribing information.



SEPTRA®

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazole

For chronic urinary tract infections in the broad sense

persistent relapsing or reinfecting cystitis, pyelitis, pyelonephritis due to susceptible organisms

- sequentially blocks two bacterial enzymes—both vital for the survival of most bacteria
- shown superior both *in vitro* and clinically to sulfamethoxazole alone[3]
- double blockade of bacterial metabolism discourages development of resistance
- rapid, high levels attained in both blood and urine
- convenient dosage: 2 tablets b.i.d. for 10-14 days

INDICATIONS: For the treatment of chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications such as obstruction.

Primarily for use in cystitis, pyelonephritis or pyelitis due to susceptible strains of the following organisms: *Escherichia coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris, Proteus morganii.*

NOTE: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

The recommended quantitative disc susceptibility method (Federal Register 37:20527-29, 1972; Bauer AW, Kirby WMM, Sherris JC, and Turck M: Antibiotic susceptibility testing by a standardized single disk method, Am J Clin Pathol 45:493, 1966) may be used for estimating the susceptibility of bacteria to Septra. With this procedure, a report from the laboratory of "Susceptible to trimethoprim-sulfamethoxazole" indicates that the infection is likely to respond to therapy with Septra. If the infection is confined to the urine, a report of "Intermediate susceptibility to trimethoprim-sulfamethoxazole" also indicates that the infection is likely to respond. A report of "Resistant to trimethoprim-sulfamethoxazole" indicates that the infection is unlikely to respond to therapy with Septra.

CONTRAINDICATIONS: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. (Before prescribing, please consult package insert.)

WARNINGS: Deaths associated with the administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but it has been reported to interfere with hematopoiesis in occasional patients. In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombopenia with purpura has been reported.

The presence of clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts should be done frequently in patients receiving Septra. If a significant reduction in the count of any formed blood element is noted, Septra should be discontinued.

At the present time there is insufficient clinical information on the use of Septra in infants and children under 12 years of age to recommend its use.

PRECAUTIONS: Septra should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency and to those with severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur. This reaction is frequently dose-related. Adequate fluid intake must be maintained in order to prevent crystalluria and stone formation. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

ADVERSE REACTIONS: For completeness, all major reactions to sulfonamides and to trimethoprim are included below even though they may not have been reported with Septra.

Blood Dyscrasias: Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic Reactions: Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis.

Gastrointestinal Reactions: Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis.

C.N.S. Reactions: Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness.

Miscellaneous Reactions: Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L.E. phenomenon have occurred.

The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents. Goiter production, diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides. Cross-sensitivity may exist with these agents. Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has produced thyroid malignancies in the species.

DOSAGE AND ADMINISTRATION: Not recommended for use in children under 12 years of age.

The usual adult dosage is 2 tablets every 12 hours for 10 to 14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	2 Tablets Every 24 Hours
Below 15	Use Not Recommended

HOW SUPPLIED: Tablets, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100 and 500 tablets and strip packages of 100 tablets, each tablet individually packed.

References: 1. Acar JF, Goldstein F, Chabbert YA: *J Infect Dis* (Suppl) *128*: 470,1973 2. Bushby SRM: *J Infect Dis* (Suppl) *128*: 442,1973 3. Data on file in the Medical Department, Burroughs Wellcome Co.

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Research Triangle Park
North Carolina 27709

Boletín

asociación médica de puerto rico

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APR 9 1976



Vol 68 Febrero 1976 No. 2

Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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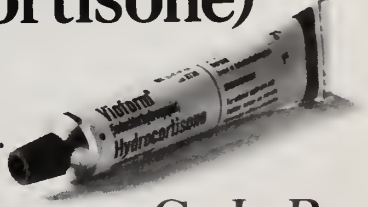
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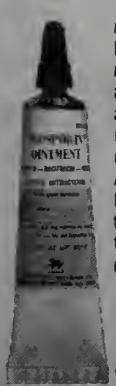
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Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS:** Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components. **WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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Breast self-examination:

KEY ROLE OF THE PHYSICIAN

item:	**Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.**
item:	**Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, *fewer than 1 in 5* women practice BSE, and *only half* have an annual breast examination by a physician.**
item:	**Only 35% of all women polled reported that a *physician* had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.**
item:	***But,* among women who received personal instruction from their physicians, the overwhelming majority *(92%)* practiced BSE during the preceding year.**

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE.

The American Cancer Society gives major emphasis to breast cancer through research and a vast array of public educational materials, designed to give women life-saving information about the disease. Our latest approach is via a pioneering television film starring Jennifer O'Neill, "Breast Cancer: Where We Are." Where we *will* be in a few years will certainly hinge on our joint efforts.

American Cancer Society®

CANCER DE PULMON: ESTUDIO COMPARATIVO DE UN HOSPITAL PUBLICO Y UN HOSPITAL PRIVADO

Abel González, MD
Víctor Lister, MD
Jorge O. Just Viera, MD

El cáncer del pulmón es la primera causa de muerte por malignidad en Estados Unidos. Su incidencia continúa en aumento, y para explicar este fenómeno se han considerado muchos factores etiológicos (1). Entre ellos sobresalen el consumo de cigarrillos y la contaminación ambiental. Otros incluyen procesos cicatrizantes del pulmón, aspiración de metales y de substancias nocivas.

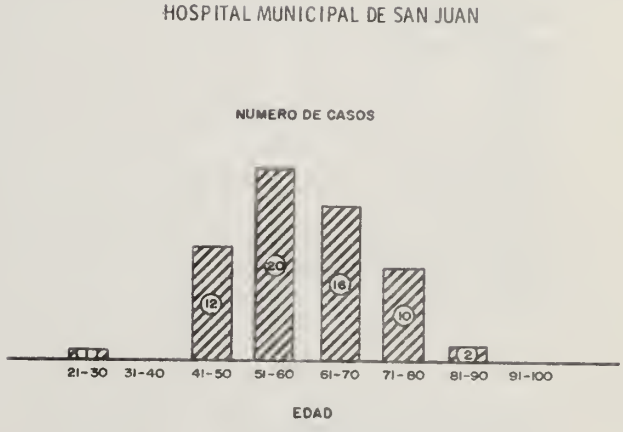
Nuestro propósito es presentar la experiencia observada con esta enfermedad en dos hospitales de San Juan. Uno, el Hospital Municipal de San Juan, atiende predominantemente a pacientes indigentes. El otro, el Hospital Auxilio Mutuo, atiende pacientes privados mayormente. En ambos hospitales se evaluaron los métodos utilizados para diagnóstico y tratamiento y se determinaron los resultados obtenidos.

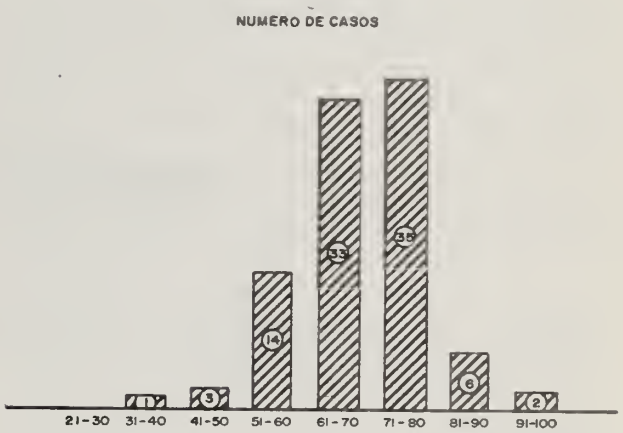
Material y Métodos

Revisamos los expedientes accesibles de 94 pacientes admitidos al Hospital Auxilio Mutuo (HAM) durante los años incluídos desde 1968 al 1974 y de 61 pacientes ingresados al Hospital Municipal de San Juan (HMSJ) durante los años desde 1968 al 1973.

Fueron clasificados los datos obtenidos del historial médico, según los criterios siguientes: edad, sexo, hábitos, medio ambiente, síntomas tempranos y tardíos, signos de diseminación intratorácica y extratorácica, las manifestaciones radiológicas, localización y tipo de tumor, los métodos utilizados para el diagnóstico, la localización de metástasis, la sobrevida y el tratamiento administrado.

La mayor incidencia ocurrió entre los 50 y 80 años de edad, con aumento progresivo, especialmente desde los 30 años. En el Hospital Municipal de San Juan los pacientes de la quinta década fueron los más numerosos, con un total de 60 por ciento. En el Hospital Auxilio Mutuo la mayor incidencia ocurrió entre los 71 a 80 años de edad; 80 por ciento. (Gráfica I). En ambos hospitales la incidencia fue 3 veces más frecuente en hombres que en mujeres.





Gráfica I

De los pacientes del HMSJ, 27 fumaban más de una cajetilla diaria de cigarrillos; 7 no eran fumadores. Los fumadores eran de menor edad que los no fumadores. En el HAM, 60 eran fumadores de más de una cajetilla de cigarrillos por día, pero 35 no fumaban en el momento de diagnosticarse el tumor. Se encontró en el HMSJ 5 pacientes con antecedentes familiares de cáncer y 3 pacientes similares en el HAM.

La Tabla I incluye los síntomas más frecuentemente en-

De la Sección de Cirugía Torácica y Cardiovascular, Hospital Municipal de San Juan, y del Departamento de Cirugía, Hospital Auxilio Mutuo, San Juan, Puerto Rico.

TABLA I

SINTOMAS Y SIGNOS MAS FRECUENTES

Síntomas	HMSJ	HAM
Tos	21	50
Dolor de Pecho	16	30
Pérdida de Peso	16	28
Disnea	13	8
Fiebre	9	20
Hemoptisis	10	18
Anorexia	8	23
Tos Productiva	7	28
Ronquera	4	2
Dedos en Palillo de Tambor	2	2
Disfagia	0	2
Signos		
Síndrome Vena Cava Superior	4	2
Sibilancias	2	8
Efusión Pleural	6	6
Cefalea	1	1
Síndrome de Horner	0	1

TABLA II

METODOS USADOS PARA EL DIAGNOSTICO

	HMSJ			HAM		
Métodos	Resultados Positivos	Total	Por Ciento	Resultados Positivos	Total	Por Ciento
Rayos X	61	61	100	94	94	100
Broncoscopía	11	24	45.8	32	34	94.1
Estudio de Citología	4	30	13.3	8	89	8.9
Biopsia Escaleno	8	26	30.7	4	14	28.5
Mediastinoscopía	0	2	0	0	0	0
Punción y Aspiración	1	1	100	0	2	0
Toracotomía	13	13	100	12	12	100
Arteriograma	0	0	0	1	4	25
Gammagrama	0	0	0	0	1	0

contrados, como la tos, dolor de pecho y pérdida de peso. Fueron igualmente afectados los pacientes de ambos hospitales, pero al considerar los síntomas de diseminación intratorácica, como lo son, la ronquera, el cuadro de obstrucción de la vena cava superior, y el derrame pleural. observamos un mayor número de pacientes afectados en el HMSJ.

El examen físico del tórax estuvo dentro de los límites normales en una gran mayoría de los casos, aunque fue impresionante en algunos pacientes la disnea y evidencia de

TABLA III

CLASIFICACION HISTOLOGICA

	HMSJ	HAM
Epidermoide	17	24
Indiferenciado	25	19
Adenocarcinoma	10	11
Ca. Células Alveolares	3	1
Carcino sarcoma	0	1
Total con Diagnóstico Histológico	55	56
Total sin Diagnóstico Histológico; Diagnóstico Clínico o Radiológico	6	38
	61	94

enfermedad crónica en otros.

El diagnóstico en muchas ocasiones tuvo base en la sospecha clínica, seguida por una placa de tórax. En el HMSJ la placa rutinaria del tórax reveló el tumor en cuatro pacientes, mientras que el HAM fueron 15 los tumores detectados así.

En el HMSJ la mayoría de los pacientes fueron referidos con un diagnóstico inicial de carcinoma del pulmón o pulmonía. Este último diagnóstico fue muy frecuente en el HAM.

La mayoría de los tumores se presentaron como masa definida en el lóbulo superior derecho o en el lóbulo superior izquierdo. En todos los pacientes los cambios radiológicos hicieron sospechar la presencia de patología pulmonar. El diagnóstico se complementó mediante el uso de tomografía y broncografía.

En la Tabla II se incluyen los métodos diagnósticos utilizados. La broncoscopía fue positiva en 46 por ciento de los pacientes del HMSJ en los cuales se practicó; en el HAM fue positiva en 94 por ciento. La citología se utilizó en 30 pacientes del HMSJ pero solo fue positiva en 4 ocasiones; en el HAM, de 89 estudios de citología hubo 8 positivos para carcinoma.

La biopsia de ganglios supraclaviculares fue positiva en 30 por ciento de los pacientes del HMSJ y en 22 por ciento de los del HAM. Cuando la biopsia supraclavicular era positiva se interpretó como metástasis a distancia que contraindicaba cirugía.

El grupo del HMSJ incluyo 46 pacientes con metástasis a distancia y 4 con metástasis locales. A solo 11 pacientes fue posible ofrecerles intervención quirúrgica curativa. En el HAM, de 94 pacientes, 53 tuvieron metástasis a distancia. En 13 hubo diseminación local al ingreso y 28 fueron intervenidos.

En el HMSJ se confirmó el diagnóstico histológicamente en 55 de los 61 pacientes; y en el HAM, en 56 de los 94. Como vemos en la Tabla III el cáncer del pulmón más frecuente en el HAM fue epidermoide. Siguió el indiferenciado. En cambio, en el HMSJ el más frecuente fue el indiferenciado, y luego el epidermoide.

El lugar de las metástasis más frecuente en los pacientes del HAM fue hueso, seguido por cerebro, mediastino, el pulmón contralateral e hígado. Diez casos presentaron metástasis después de cirugía. En el HMSJ las metástasis por orden de frecuencia fue, primero a pleura, luego mediastino, ganglios supraclaviculares, cerebro, hígado, tiroide y hueso.

La Tabla IV incluye el tratamiento instituído. Este varió según los hallazgos. En el HAM, 28 pacientes fueron operados. De éstos, 6 recibieron radioterapia; 1 quimioterapia; y 3 radioterapia y quimioterapia combinada como tratamiento adicional a cirugía. A 43 pacientes adicionales se le administró radioterapia paliativa y nueve recibieron tratamiento combinado de radioterapia y quimioterapia sin cirugía y un solo paciente recibió quimioterapia únicamente. No recibieron tratamiento alguno 23 pacientes debido al estado avanzado de su enfermedad. En el HMSJ, 15 pacientes fueron operados, pero solo en once la intervención fue curativa. A 4 pacientes quirúrgicos se les administró tratamiento adicional con radioterapia y quimioterapia. Recibieron radioterapia solamente 18 pacientes y 3 pacientes fueron tratados con quimioterapia. No recibieron terapia alguna 25 pacientes con enfermedad avanzada.

La sobrevida promedio en los pacientes operados del HAM fue 24.8 meses. Encontramos 3 pacientes operados con más de 5 años de sobrevida (3 por ciento). En el HMSJ, el promedio de sobrevida en los pacientes sometidos a tratamiento quirúrgico curativo fue de 25 meses, 2 con sobrevida de 2 años a pesar de enfermedad diseminada; uno con 3 años de sobrevida sin evidencia de metástasis y uno con sobrevida de 5 años (1.5 por ciento). En ambos hospitales el promedio de sobrevida con tratamiento paliativo fue de 6 meses; y sin tratamiento, de 2 meses.

TABLA IV

TRATAMIENTO

	HMSJ	HAM
Cirugía Curativa	11	18
Cirugía Paliativa	4	10
Paliativo (Radioterapia y/o Quimioterapia)	21	43
Sin Tratamiento	25	23

Discusión

Es ya innegable la relación entre cáncer del pulmón, el cigarrillo, y la contaminación ambiental (2) (3). En nuestro estudio hemos incluído un hospital privado y uno gubernamental para obtener una visión más amplia del diagnóstico y tratamiento de esta enfermedad en Puerto Rico. Aunque tanto los pacientes privados como los indigentes presentaron síntomas iniciales similares, síntomas que ya apuntan a una etapa avanzada, los pacientes indigentes del HMSJ tuvieron una frecuencia mayor de síntomas causados por diseminación intratorácica, y por lo tanto, de incurabilidad. Es posible que aquí exista terreno fértil para los educadores en asuntos de la salud, porque, ¿será esta tardanza del indigente en acudir para tratamiento temprano una falla en su educación, o será problema de tardanza en ser referido al HMSJ por el sistema de salud a nivel de cuidado primario? No lo sabemos. Sí sabemos que en el HAM, donde existe un plan prepagado con servicios fácilmente asequibles a los socios del plan, y donde los pacientes son ingresados por sus propios médicos, el número de casos detectados por placa rutinaria del tórax fue casi cuatro veces mayor que en el HMSJ.

Esta experiencia subraya la importancia del examen radiológico rutinario del tórax en las décadas críticas del padecimiento, de los 40 años en adelante. Es imprescindible que el médico acepte como médida de éxito terapéutico nada menos que una placa de pecho completamente normal en cualquier paciente de edad crítica con síntomas pulmonares, especialmente si son fumadores. Fueron numerosos los pacientes en este estudio tratados por "pulmonía" durante meses cuando padecían de un cáncer pulmonar. En esta serie no encontramos casos de cáncer del pulmón con radiografía normal del tórax.

Es casi imposible determinar cuando comienza el proceso maligno porque antes de su primera manifestación radiológica o síntomas, puede estar presente por meses e incluso años. Algunos hablan de veinte meses como promedio (4). Nuestro estudio confirmó nuevamente predominio de hombres sobre mujeres en esta enfermedad.

Resulta difícil de explicar la diferencia en rendimiento por broncoscopía en ambos hospitales. Fue de 46 por ciento en el HMSJ y 94 por ciento en el HAM, aunque el tipo histológico más común en cada hospital fue diferente. La selección de los pacientes para este examen quizás resultó importante.

En cambio, la ayuda brindada por el examen citológico del esputo y de los lavados bronquiales fue escasa, con 8 por ciento y 13 por ciento de estudios positivos en el HAM y el HMSJ respectivamente. Esto sugiere que la confiabilidad de este estudio, según se practica en Puerto Rico, es muy baja. En otros centros se han informado por cientos de positividad hasta de 52 por ciento con 2 muestras, 69 por ciento con 3 y 76 por ciento con 5 muestras (5).

Fue sorprendente que la biopsia de ganglios supraclaviculares tuviese un rendimiento diagnóstico mayor que la citología.

El tipo histológico más frecuente en el HMSJ fue el indiferenciado. En el HAM el epidermoide resultó el tipo más frecuente, una situación similar a la informada en el estudio del Hospital Universitario de Puerto Rico, (6) en el cual el epidermoide fue más frecuente.

Aproximadamente 20 por ciento de los pacientes en ambos hospitales presentaron la enfermedad localizada. Esto coincide con el estudio del Hospital Universitario ya mencionado y con los informes en la literatura (6) (1). La sobrevida de los pacientes con

tratamiento paliativo (radioterapia y quimioterapia) fue de 6 meses en ambos hospitales mientras que los pacientes no tratados sobrevivieron solo 2 meses. Estas cifras son similares a las obtenidas en otros estudios (7). El mejor método de tratamiento aún es la cirugía. Se practicaron 27 lobectomías y 12 neumonectomías. No hubo mortalidad post-operatoria y la morbilidad fue mínima.

La sobrevida a 5 años fue 1.5 por ciento en el HMSJ y de 3 por ciento en el HAM. La sobrevida a 5 años informada en el Hospital Universitario, fue 3 por ciento (6). Esto subraya que la sobrevida de cáncer del pulmón en Puerto Rico es mucho menor que la usualmente informada en la literatura (7).

Resumen

Fueron revisados los expedientes médicos de los pacientes con cáncer del pulmón que ingresaron en los Hospitales Auxilio Mutuo y Municipal de San Juan. Se compararon los resultados con un informe similar anterior del Hospital Universitario de Puerto Rico y con los de la literatura mundial.

La sobrevida y mortalidad han variado muy poco en los últimos años. La Cirugía constituye en la actualidad el método más eficaz para aumentar la sobrevida. Los métodos paliativos no prolongan la vida aunque ofrecen mejoría sintomática.

Los resultados de citología fueron bajos en ambos hospitales. En el Hospital Municipal de San Juan se encontró un tipo de tumor predominante de mayor agresividad, distinto al encontrado en los pacientes del Hospital Auxilio Mutuo, lo que posiblemente explica una sobrevida menor.

En los pacientes del Hospital Auxilio Mutuo el diagnóstico se hizo más temprano.

La sobrevida a 5 años en Puerto Rico para cáncer del pulmón, tanto en hospitales gubernamentales como en la práctica privada, es menor que la informada en la literatura.

Summary

The results of treatment of lung cancer in patients admitted to the Auxilio Mutuo Hospital and the San Juan Municipal were reviewed. They were compared with previous reports from the University Hospital of Puerto Rico and from the literature.

Long term survival from all three hospitals was less than 3 percent at five years. Surgery is the most effective treatment at the present time. Radiotherapy and chemotherapy relieved symptoms without prolonging life.

We found that indigent patients from the Municipal Hospital had more malignant tumors than those from the Auxilio Mutuo. In private patients from the Auxilio Mutuo the diagnosis was reached earlier in the course of the disease.

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ASSESSMENT OF VITAMIN B_{12} ABSORPTION IN TROPICAL SPRUE UTILIZING A WHOLE BODY COUNTER

José J. Corcino, MD
René Dietrich, MD
Aldo E. Lanaro, MD

Several methods have been described for the assessment of labeled vitamin B_{12} absorption in humans (Table I). Of all of these, the Schilling test has proved to be the most valuable for routine clinical purposes. It has, however, several disadvantages, the principal one being that the administration of 1000 ug of vitamin B_{12} parenterally as a "flushing" dose precludes the proper evaluation of response to other modalities of therapy. To avoid this limitation we have adopted the use of a whole body counter to assess the absorption of this vitamin. The present communication contains the results obtained with this technique.

Materials and Methods

Subjects – Thirty-eight Puerto Rican subjects were investigated: 26 patients with overt, untreated tropical sprue and 12 asymptomatic subjects.

Techniques utilized for the laboratory evaluation of intestinal function and structure in the tropical sprue subjects were similar to those described in previous communications from this laboratory (1, 2).

Technique – The Puerto Rico Nuclear Center whole body counter (Packard) consists of four 6" x 6" NaI (TL) crystal detectors. These detectors are connected to an amplifier and a 4096 channel pulse-height analyzer computer. The crystal detectors are located in a shielded room 7 x 7 x 7.5 feet constructed with 6 inches of steel, lined with lead and tin. Patients were counted for 10 minutes in a table placed in a fixed position between the four detectors.

The ^{57}Co labeled vitamin B_{12} and the intrinsic factor capsules were purchased from Mallinckrodt Nuclear. Each capsule of ^{57}Co B_{12} contained approximately 0.5 ug of the labeled vitamin with a specific activity of 1 uCi/ug. The intrinsic factor capsules contained 60 mg of porcine intrinsic factor. Both capsules were administered simultaneously to each subject after an overnight fast. Total body radioactivity was determined before and immediately after the administration of the capsules. The difference between both counts was taken as the 100 percent value. Total body radioactivity was again determined 7 days afterwards and the percent retained over this period of time estimated. The results of the preliminary studies performed to determine the time at which a plateau was attained are described below.

Results

Biochemical and Absorption Studies. All the tropical sprue subjects had xylose malabsorption; steatorrhea was present in 22 out of the 26 subjects; all had megaloblastic anemia and low serum folate levels; 20 out of 26 also had low serum B_{12} levels. Jejunal mucosal abnormalities were present in all.

Vitamin B_{12} Absorption. The results obtained in the preliminary studies aimed at determining the optimal time at which total body radioactivity stabilized are shown in Figure 1. As shown, by the end of 7 days, a plateau had been reached in both control and tropical sprue subjects.

The results depicted in Figure 2 represent, therefore, the percent radioactivity retained by control and tropical sprue subjects 7 days after the administration of the ^{57}Co B_{12}. Retention of radioactivity was 55 ± 29 percent (mean ± 2 SD) and 9.6 ± 13.4 percent (mean ± 2 SD) for the control and the tropical sprue subjects, respectively.

From the Puerto Rico Nuclear Center and the General Clinical Research Center, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

This work was supported by grants from the Research Corporation, New York City; Grant RR-63-13 from the General Clinical Research Center, Program of the Division of Research Resources, National Institutes of Health, Bethesda, Maryland; and the Academic Career Development Award No. 5 K07-AM 70696-02 (Dr. José J. Corcino). The paper was prepared in connection with work under contract No. AT-(40-1) 1833 with U. S. Atomic Energy Commission. The Commission retains a non-exclusive royalty-free license in and to any copy rights covering this paper, with the right to authorize others to reproduce all or any part of the copyrighted paper.

Address requests for reprints to: Dr. José J. Corcino, General Clinical Research Center, Medical Sciences Campus, GPO Box 5067, San Juan, P. R. 00936.

TABLE I
METHODS FOR THE DETERMINATION OF VITAMIN B_{12} ABSORPTION

(1) Determination of radioactivity in feces after the administration of labeled vitamin B_{12} (Heinle, Welch) (7)
(2) Determination of radioactivity in urine (Schilling) (6)
(3) Quantification of liver uptake (Glass) (8)
(4) Determination of radioactivity in plasma (Booth, Mollin) (9)
(5) Utilization of the whole body counter (Reizenstein, Cronkite, Cohn) (10)

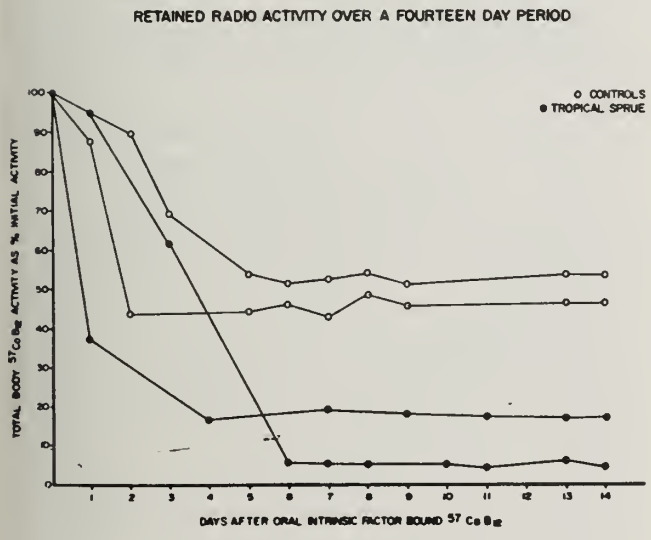


Figure 1

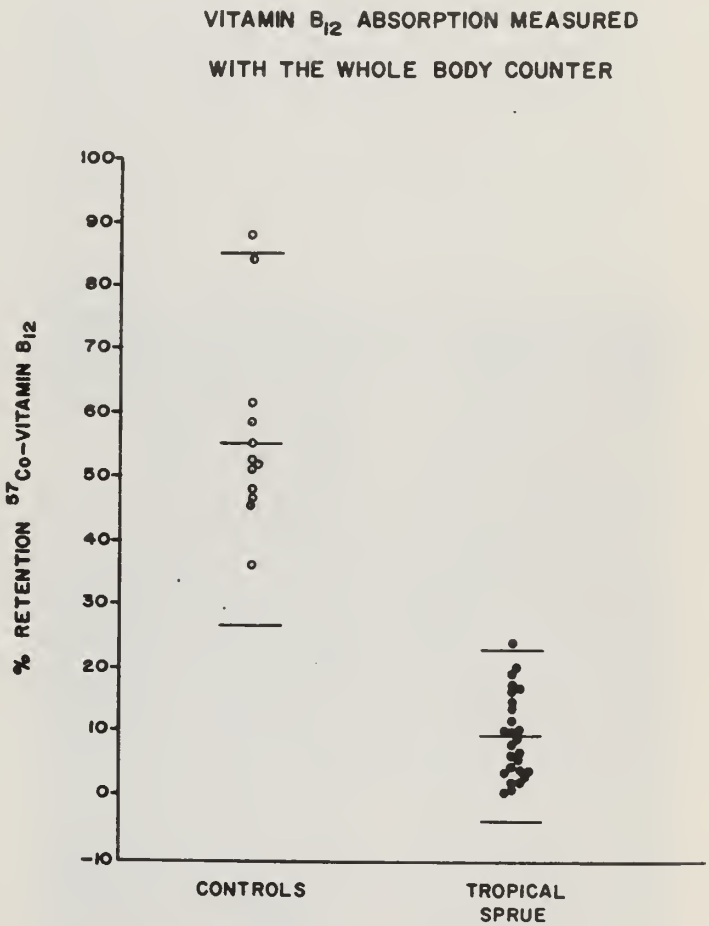


Figure 2

Discussion

Deficiency of vitamin B_{12} due to malabsorption is present in nearly all subjects with tropical sprue (3, 4). Such malabsorption has been attributed heretofore to impairment of ileal absorptive capacity.

The introduction of radioactive cobalt labeled vitamin B_{12} in 1950 (5) led to the development of different methods to study absorption of this vitamin in man. Table I summarizes the most commonly utilized techniques. The most widely used method for measuring vitamin B_{12} absorption is the urinary excretion test or Schilling (6). A major disadvantage of this test is that large quantities (1000 ug) of vitamin B_{12} given as "flushing doses" usually result in a hematopietic response, precluding subsequent attempts at eliciting responses with other therapeutic agents.

A whole body counter permits the study of vitamin B_{12} absorption utilizing small doses of the vita-

min. One of the difficulties encountered in the use of a whole body counter with four NaI crystals is its calibration. The administration of a dose of labeled vitamin B_{12} results in substantial variation in the distribution of the labeled vitamin within the body as a function of time, especially in the first two hours when the capsule is being dissolved. This change in the geometry results in a variation in the initial count rate of the subjects, so that one should take as the 100 percent the count rate present immediately after the administration of the dose. At this time most of the radionuclide is in the stomach and, therefore, has a closer geometry to the seven day count rate when most of the absorbed vitamin B_{12} is in the liver.

The present communication contains our experience in the assessment of vitamin B_{12} absorption in tropical sprue utilizing a whole body counter. This technique is, in our hands, reliable and sensitive. A clear cut separation is obtained between the control subjects and the tropical sprue patients. It has the added advantage that it has allowed us to investigate the response in vitamin B_{12} absorption to various therapeutic agents. The results concerning this response will be the subject of subsequent reports.

Summary

Absorption of ^{57}Co vitamin B_{12} intrinsic factor complex was assessed in 12 control and 26 tropical sprue subjects utilizing a whole body counter. Mean 7 day retention was 55 ± 29 (mean ± 2 SD) and 9.6 ± 13.4 (mean ± 2 SD) for the control and tropical sprue subjects, respectively. This technique is highly reliable and reproducible for the assessment of vitamin B_{12} absorption in this syndrome.

Resumen

La absorción del complejo ^{57}Co vitamina B_{12} factor intrínsico fue medida en 12 sujetos controles y 26 pacientes con esprú tropical utilizando un contador de cuerpo entero. La retención promedio a los 7 días del isótopo fue 55 ± 29 para los sujetos controles y 9.6 ± 13.4 (promedio ± 2 desviaciones standard) para los pacientes con esprú tropical. La técnica utilizada es confiable y reproducible en la determinación de la absorción de la vitamina B_{12} en el esprú tropical.

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DIFFUSE ESOPHAGEAL SPASM

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Diffuse esophageal spasm is diagnosed when the orderly progression of peristalsis is interrupted by areas of isolated, irregular, strong, non-propulsive contractions. These isolated but multiple irregular muscular spasms may cause substernal pain. By arresting the downward movement of the swallowed bolus they may cause partial regurgitation and tracheal aspiration. Manometric measurements demonstrate replacement of normal peristaltic waves by stationary, synchronous, high amplitude contractions.

The roentgen appearance of diffuse spasm is commonly seen in older people in the absence of symptoms. More important is its distinction from achalasia and esophageal carcinoma. Dynamic studies clearly demonstrate in achalasia the absence of lower sphincter relaxation; there are weak and ineffective esophageal contractions with delay of esophageal emptying. Localized, irreversible esophageal stenosis with an irregular fixed wall suggests malignancy.

We report here the occurrence of diffuse esophageal spasm associated with severe pharyngeal dysfunction and tracheal aspiration. The esophagogram suggested at first-sight esophageal carcinoma in the middle third of the esophagus. The diagnosis was established by cine-roentgenogram.

Case Report

A sixty-six year old female was admitted to the Mayagüez Medical Center on August 1974 with dysphagia, weight loss and chronic productive cough. The patient had smoked one pack of cigarettes per day for 35 years. Seven months previously she suddenly developed severe episodic substernal discomfort and difficulty in swallowing cold liquids and solids. The patient was afraid to eat: the discomfort was frequently associated with hoarseness and severe paroxysms of cough.

There was no familiar or past history of diabetes, parkinsonism, central or peripheral neuropathy, myopathy or cerebrovascular disease.

On physical examination the temperature was 36.5° C, pulse 80 per minute and regular, respiratory rate 20 and blood pressure 130/90 mmHg. She was alert and cooperative, but was extremely emaciated, weighing 30 pounds less than her expected weight of 96 pounds. Medium-moist expiratory rales



Fig. 1: *Esophagogram showing narrowing in the middle third of the esophagus suggesting carcinoma.*

From the Mayaguez Medical Center, Mayaguez, Puerto Rico.

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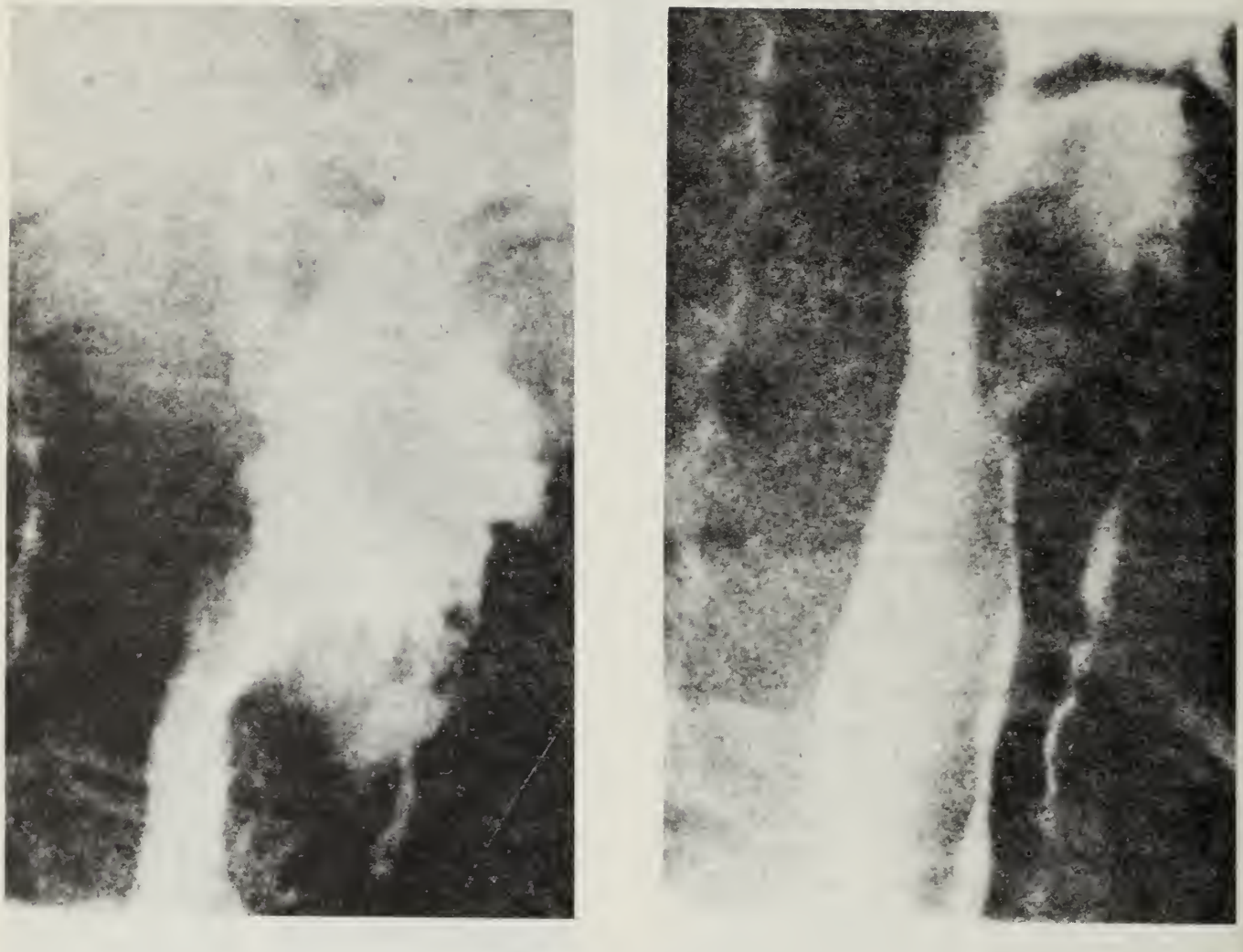


Fig. 2: *Frames of a cineroentgenogram showing: A. Asynchronous contraction of upper esophageal sphincter. Barium is flowing into the esophagus and trachea at the same time. B. Barium filled esophagus and aspirated contrast media coating the tracheal wall.*

were heard at both lung bases posteriorly. There were no neurologic abnormalities. The hemogram, urinalysis, serum electrolytes and chemistries were within normal limits. A chest film showed a pneumonic density of 4 x 6 cm. localized mostly in the superior segment of the lower lobe in the right lung. Tomography and bronchography did not demonstrate bronchial encroachement and cytologic examinations of 3 sputa were negative for malignant cells. An esophagogram revealed a filling defect in the middle third and slow progression of the bolus of barium in the middle and lower third of the esophagus (Fig. 1). Endoscopy on two occasions failed to demonstrate an esophageal obstructive lesion.

Suspecting a disorder of motility to account for the bizarre esophagogram, a cine-roentgenogram was performed. There was muscular incoordination and delayed relaxation in the superior third of the esophagus. Cough was produced, irregular pharyngeal contractions and tracheal aspiration was demonstrated each time the patient swallowed barium (Fig. 2). These physiologic events were manifested by substernal pain and, of course, by severe paroxysms of cough. The bolus of barium progressed imperfectly with many ineffective tertiary waves in the middle and lower third of the esophagus (Fig. 3). The patient was discharged five weeks after admission on a tranquilizer and advised to eat small meals slowly. There was no symptomatic improvement. She was readmitted to the Department of Surgery one month later to evaluate the possibility of esophageal myotomy, but died preoperatively of bilateral bronchopneumonia. At autopsy only bilateral bronchopneumonia was found. There were no abnormalities of the esophagus.



Fig. 3: *Frame of a cine-esophagogram showing simultaneous contractions of various segments in the middle and lower esophagus.*

Comment

The earliest description of diffuse esophageal spasm (D.E.S.) included a group of patients with painful and intermittent dysphagia (1). Radiology, cine-fluoroscopy and esophagomanometry have permitted the separation of these conditions from other causes of esophageal obstruction. Although little is known about the pathogenesis of this disorder, hypertrophy of esophageal muscle is reported in a few instances. Electron microscopic examination has shown generalized degenerative changes of the vagal esophageal nerves, in some cases (2). Diffuse esophageal spasm occurs particularly in elderly persons. The substernal pain is generally associated with a disruption of normal peristalsis and an inability to swallow, the pain may be intermittent and related to stress; it can be severe enough to mimic ischemic heart disease. The patients seem to be sensitive to the effects of temperature: hot water tends to relieve the painful attacks, and cold water to precipitate them (3).

Radiologically the extent and severity of esophageal abnormalities vary widely from the presence of tertiary waves (irregular non-propulsive contractions), to arrest of the swallowed bolus, to partial regurgitation and endotracheal aspiration. These dynamic events are most clearly apparent by cine-roentgenography. When extreme in degree the disordered motility causes the barium-filled lumen to appear on roentgenograms in the form of a spiral coil (corkscrew appearance) or in a series of almost-closed compartments resembling beads (rosary appearance). Esophageal pressure measurements show the normal pattern of peristaltic contractions replaced by stationary simultaneous contractions of various segments of the esophagus. At esophagoscopy the absence of abnormalities is the rule, although occasionally narrowed segments may be demonstrated. Some patients have relatively high pressure in their lower esophageal sphincters (4).

Disorders of contractility at times radiographically identical to diffuse esophageal spasm, can occur in the following disorders: cerebrovascular disease, parkinsonism, amyotropic lateral sclerosis, multiple sclerosis, peripheral neuropathy, thyrotoxic myopathy and myotonic dystrophy (5-6). In diabetes mellitus, tertiary wave contractions are not uncommon.

In the treatment of diffuse esophageal spasm, reassurance, the avoidance of cold or carbonated beverages and eating in an environment free of tension may be useful. Sometimes nitroglycerine gives prompt relief of the spasm (7). Anticholinergics and topical anesthetics are not consistently beneficial. If dysphagia is severe pneumatic dilatation of the cardia at times helps relieve symptoms (8), although no change in esophageal measurements or in the esophagogram may be demonstrated (9). In those patients whose symptoms are truly disabling an esophagomyotomy should be considered.

Dysphagia is a serious symptom and its presence calls for meticulous investigation. The diagnosis of diffuse esophageal spasm is a diagnosis of exclusion and can be made only when no local organic cause of dysphagia is found after appropriate studies. Certain patterns of abnormal swallowing occurs frequently in specific disease states, abnormalities may be detected in the barium swallow or esophageal fluoroscopy, but

these simple techniques are generally inadequate in demonstrating complex swallowing disturbances. Abnormalities which go unnoticed during fluoroscopy may be easily detected by analysis of cine-films. It is suggested that cine-roentgenographic studies be used routinely in studies of esophageal dysfunctions.

Summary

A patient with diffuse esophageal spasm is presented who was admitted to the hospital because of substernal pain on swallowing, weight loss and a chronic productive cough. The static roentgenograms were suggestive of esophageal carcinoma but no obstructive lesion was found on two endoscopies or at autopsy. A cine-roentgenogram clearly demonstrated the dynamics of esophageal spasm and repeated bronchial aspiration. The characteristics of this form of esophageal dysfunction are discussed. The diagnostic usefulness of the cine-roentgenogram is emphasized.

Resumen

Se presenta un paciente con espasmo difuso del esófago hospitalizado por dolor subesternal cuando tragaba, pérdida de peso y una tos crónica y productiva. El esofagograma simple sugirió un carcinoma del esófago pero no se encontró lesiones obstructivas en dos endoscopías ni más tarde en la autopsia. Un estudio radiocinematográfico demostró claramente la dinámica del espasmo esofágico y de las aspiraciones bronquiales repetidas al tragar. Se discuten las características de este tipo de disquinesia esofágica. Se demuestra la utilidad diagnóstica de la radiocinematografía.

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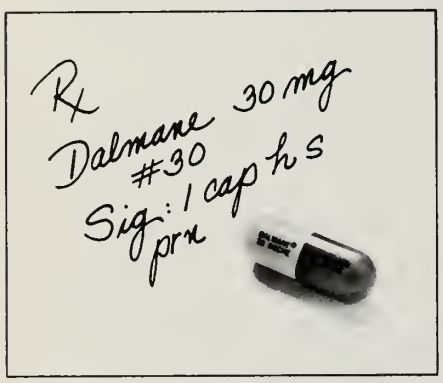
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Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

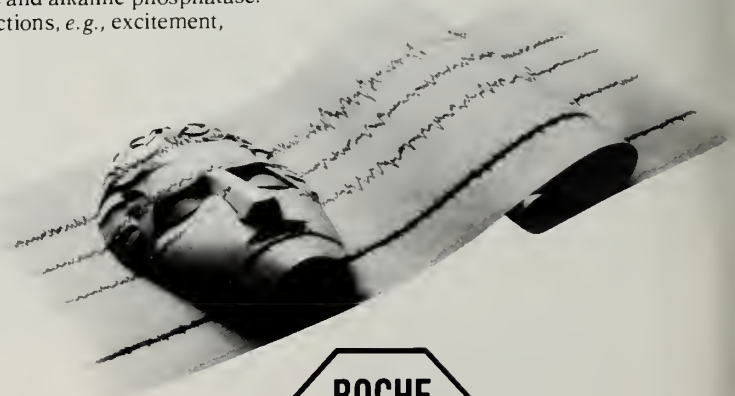
Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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FOCAL NODULAR HYPERPLASIA OF THE LIVER

Case Report with Unusual Radiographic Presentation

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Queenland Morales, MD

Focal nodular hyperplasia of the liver is a rare tumor like entity, the diagnosis and malignant potential of which has been frequently debated in the medical literature (1, 2, 3). In the opinion of Malt (1) a gradation is felt to exist between focal nodular hyperplasia, multiple adenomas, and carcinoma. Adhering to the rigurous criteria of Edmonson's classification of tumors of the liver, (4) only three such lesions were seen at the Massachusetts General Hospital, (1) in a period of 20 years and interestingly all three cases were incidental findings at the time of abdominal surgery for other unrelated reasons.

We would like to present a unique case of this entity in which the lesion was causing considerable



Figure 1



Figure 2

From the Department of Radiology, I. González Martínez Oncologic Hospital and Diagnostic Radiology Department, Centro Médico de Puerto Rico.

symptomatology and in which gross radiographic abnormalities were present.

A 26-year old, Gr. 11, P. 11, Ab. 0, female was referred to the I. González Martínez Oncologic Hospital because of a 5 month history of localized epigastric burning pain initially relieved by antiacids, but accompanied in the past several weeks by post prandial vomiting. Past history, review of systems, and physical examination were unremarkable, except for the patient's ectomorphic habitus which she relates to have been essentially unchanged in over 10 years. A hemoglobin of 11.4 grams was the only abnormal laboratory findings. A chest X-ray was normal. An upper G. I. Series was performed on 1-9-75 and demonstrated a huge extrinsic pressure effect upon the gastric cardia (figures 1 and 2) interpreted as being a predominantly extrinsic gastric tumor such as a leiomyoma or a leiomyosarcoma. The mass effect upon the barium filled stomach was reflected in all views.

Exploratory laparotomy was performed on 1-22-75 and demonstrated a multi-lobulated, 8 x 8 cms. lesion confined to the left lobe of the liver. No intrinsic gastric abnormality or evidence of other intra-abdominal pathology was found. A left lobe sequestrectomy was performed and the pathology findings were those of focal nodular hyperplasia of the liver fulfilling all of Edmonson's criteria for this diagnosis.

The patient made an uneventful recovery and is at present (August 1975) asymptomatic. A follow up upper gastro intestinal series performed on May 1975 showed no gross intrinsic or extrinsic abnormality of the stomach.

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NOTA

EL ARTICULO "ASPECTOS QUIRURGICOS DEL IMPLANTE DE MARCAPASOS - REPORTE DE TRES CASOS

Por un error en la edición de octubre 1975 aparece publicado el artículo "Aspectos Quirúrgicos del Implante de Marcapasos - Reporte de Tres Casos de Marcapasos Implantados" cuando debe leer solamente "Aspectos Quirúrgicos del Implante de Marcapasos".

TRICHOPHYTOBEZOAR OF THE ENTIRE SMALL INTESTINE: REPORT OF A RARE COMPLICATION

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Bezoars are conglomerated masses of various foreign or intrinsic substances which may be found in the stomach and intestines of both men and animals. Their presence cannot be taken lightly since, if untreated, they can lead to severe complications such as obstruction, inanition and exhaustion, irritation of the stomach or bowel wall, mucosal erosion, bleeding, ulceration, perforation, peritonitis, and even death. Bezoars can be classified according to their constituents as follows: trichobezoars are balls of hair; phytobezoars are balls of fibers of vegetable matter; trichophytobezoars are combinations of both; other bezoars made up of concretions, fungi, yeast, or food have also been described.

We recently observed an 18-year old girl with a trichophytobezoar of the entire small intestine extending from the duodenum to the distal ileum. This very rare case is reported because of its interest and to point out some of the pitfalls which may occur in the diagnosis and treatment of this condition.

Case Report

Clinical Presentation:

An 18-year old deaf-mute and mentally retarded girl had been intermittently admitted to the State Psychiatric Hospital for counselling and care. She was admitted to the University District Hospital on December 16, 1973 with abdominal pain, vomiting, and diarrhea of about three days duration. She came accompanied by relatives who did not contribute any pertinent social or psychiatric history except that she had had meningitis at the age of two years, and occasional convulsions until four years prior to admission. No information was available regarding diet, anorexia, weight loss, or personal habits. On physical examination we observed a severely retarded girl who was uncooperative and appeared dehydrated and chronically ill. Head and chest were normal and pertinent findings included moderate tympanitic distension of the abdomen and severe generalized tenderness especially in the right lower quadrant. A "fullness" could be felt in the latter area. Rebound tenderness was not present. Hyperperistalsis and rushes could be heard. Laboratory work-up included an amylase of 111 Somogyi units; WBC 13,400 with 75 PMN; sodium 139 mEq/L; chloride 96 mEq/L; potassium 5.3 mEq/L; CO_2 19 mEq/L. X-rays revealed gas distention and occasional air-fluid levels throughout, suggestive of ileus but also compatible with partial mechanical obstruction.

Hospital Course:

The clinical impression on admission was that of acute perforated appendicitis with early appendiceal abscess. Accordingly, the patient was admitted to the surgical ward and placed on intravenous fluids, nasogastric suction, and intravenous antibiotics (Keflin). With this treatment the patient failed to improve and twelve hours after admission she developed a board-like, rigid abdomen.

Laparotomy was done with a pre-operative diagnosis of intestinal obstruction with perforation and peritonitis. The small bowel was markedly distended. The bowel wall was hyperemic and swollen, and on palpation, it had a doughy consistency. On manipulation of different segments of the small intestine, the manipulated segment retained whichever form or angle was given by the surgeon. This was seen throughout the small intestine down to the distal ileum. About 300 to 400 cc of yellowish ascitic fluid was found in the peritoneal cavity. Large mesenteric nodes were also present. The appendix was normal. The liver was large, pale and edematous. With these findings, the original diagnosis of intestinal obstruction and secondary peritonitis was not tenable. The bowel wall was so thick and inflammed, that the operating surgeons believed the primary pathology to be granulomatous enteritis (Crohn's Disease). Because of the extent of the involvement and the notorious difficulty in healing of these patients, the surgeons decided not to biopsy or open the bowel. A lymph node biopsy was taken. The post-operative diagnosis was partial intestinal obstruction secondary to granulomatous enteritis, and possibly ascariasis.

From the Departments of Surgery, Surgical Research Laboratories, and Pathology, of the University of Puerto Rico Medical School and the Puerto Rico Medical Center.

Supported in part by a special Grant from The Good Samaritan Foundation to the Surgical Research Laboratories.

After operation she ran an afebrile uneventful course during the first three days. On the third post-operative day she developed diarrhea which was treated with intravenous fluids and oral Lomotil. On the seventh post-operative day she developed abdominal distension, tachycardia and hypotension. She vomited, aspirated and developed cardiac arrest. Attempts at resuscitation were unsuccessful.

Autopsy:

Pathological examination showed an emaciated body with evidence of severe chronic malnutrition and superficial sacral ulcers. The thoracic cavity was unremarkable. Most abnormal findings were confined to the abdominal cavity, which contained approximately 900 cc of yellow fluid mixed with fibrinous material. The peritoneum was rough and hyperemic, and partially covered by a fibrinous purulent exudate. The intestinal loops were markedly dilated and firm on palpation. The loops were hard and doughy as they had been found at the time of surgery. Approximately 150 cm from the ileocecal valve there was a 4 cm x 1 cm area of perforation of the wall, through which one could see hair and thread inside the bowel. The bowel was opened longitudinally with the following findings: a small ulcer at the pylorus; a large area of ulceration at the ampulla of Vater; impacted masses of hair, thread and vegetable particles in the jejunum and ileum. Trichuris trichiura were also seen within this mass. The colon contained liquid fecal material.

The pathologic diagnosis was: 1) intestinal obstruction due to trichophytobezoar with perforations and generalized peritonitis; 2) Ascites; 3) Focal aspiration pneumonia and focal atelectasis; 4) "Peptic ulcers" of the pylorus and duodenum; 5) Fatty metamorphosis of the liver.

Discussion

Trichobezoars are masses of hair firmly matted together and covered with a thick coating of mucoid substance. Entwined with the hair one may find particles of all kinds of food, particularly fat which is not digested by the gastric juices, as well as different filamentous substances of vegetable origin. Fermentation, putrefaction and decomposition of the various foods and organic residues accounts for the characteristic putrid odor of these masses, indicative of their high bacterial content, of importance in causation of a high mortality. The most frequent organisms found are gram negative bacteria and Clostridiae.

Phytobezoars are composed of fibers of vegetable origin, and are commonly found in men in their fifth and sixth decades. Predisposing factors for the development of phytobezoars include (1) continuous ingestion of substances with high cellulose content; (2) improper mastication and rapid deglutition; (3) edentia; (4) post-gastrectomy state; (5) any natural or acquired narrowing of the intestinal lumen.

Trichobezoars are characteristically found in females (90 percent), in the second or third decades (80 percent), who have "hair-biting" and other neurotic habits and even psychoses. They are a manifestation of a personality maladjustment although not necessarily of psychosis. They are most commonly found in the stomach, but can also be found anywhere in the gastrointestinal tract down to the anus. Colonic obstruction by trichobezoars has been reported. Frequently trichobezoars cause pyloric obstruction and sometimes they achieve such an enormous size that they completely fill the gastric cavity. Occasionally a bezoar may coincide with a gastric carcinoma. Small intestinal bezoars are quite rare, and the complication of small intestinal perforations has been reported only twice before (3).

Symptoms are non specific (1). Epigastric pain, nausea, vomiting, constipation, loss of weight and occasionally hematemesis and melena occur. Clinical findings are frequently compatible with obstruction of the gastrointestinal tract at any level. A palpable, movable abdominal mass is a very characteristic finding. Crepitation may be felt over the mass in cases of trichobezoar. Ascites in the late stages is a common finding. Putrid halitosis is also frequently found. Laboratory findings may include: (a) anemia, usually nutritional; (b) hypoproteinemia, both nutritional and as result of a protein-losing enteropathy; (c) leukocytosis depending on complications. A final pre-operative diagnosis is either made radiologically or by gastroscopy when the bezoar is intragastric. Plain films of the abdomen usually show a pattern of finely mottled air interspaced within an otherwise homogenous density. A barium swallow may be diagnostic in gastric bezoars, where large, smooth filling defects are seen. Prognosis depends on early diagnosis and the presence of complications (2). Factors which may help establish an early diagnosis are a high index of suspicion, and appropriate X-ray studies.

Our patient had all the reported complications: ulcers, anemia, hypoproteinemia (4), intestinal obstruction, ascites, peritonitis, perforation, and death (2, 3). Trichobezoars are accompanied by complications in 53 percent of the cases with a mortality rate of 50 percent for patients treated non-operatively. If perforation exists the mortality rate is 100 percent. The incidence of intestinal and gastroduodenal ulceration is higher for phytobezoar than for trichobezoar but the latter are much more lethal. The incidence of perforation is more or less the same for both, but again, trichobezoars are more lethal.

Adequate therapy means surgical removal of the trichophytobezoar. In the pre-operative preparation

emphasis should be placed on adequate hydration and antibiotic coverage for both gram negative and gram positive organisms. During operation, meticulous care should be taken not to spill the contents of the bezoar into the peritoneal cavity, because of its high effective potential. A thorough exploration of all abdominal viscerae should be carried out, keeping in mind that multiple masses may coexist at different levels of the G. I. tract. Careful peritoneal lavage should be done. Occasionally, systematic chemical degradation of gastric bezoars can be successful if the bezoar is composed of cellulose or other biodegradable material. In the case of trichobezoars this is not so. For the latter, surgical removal is the mainstay of treatment.

Our case illustrates the severe difficulty in diagnosing this condition. Even during surgery, lack of suspicion led to an erroneous diagnosis. Grossly this disease may mimic other conditions of the GI tract. Thus, the key factor for early diagnosis is a high index of suspicion. It is paramount to look for early signs, since the later complications of gastritis, bleeding, perforation, or peritonitis will invalidate most signs and confuse the picture as it did in our case. The type of patient and the presence of peculiar personal habits can contribute to suspicion of the correct diagnosis.

Summary and Conclusions

We have presented the case of an 18-year old girl who was mentally deficient and deaf-mute. The history was impossible to obtain. She presented an acute abdomen which progressed to a frank peritonitis. Abdominal exploration showed severe chronic inflammatory changes of the small bowel wall which grossly simulated granulomatous enteritis. The patient expired on the seventh post-operative day from bowel perforation and aspiration of gastric contents. Autopsy showed a trychophytobezoar of the entire small intestine with multiple ulcers and perforations. The clinical picture and main diagnostic factors of trichophytobezoars are discussed. The key factor in diagnosis is a high index of suspicion especially in a particular sub-group of patients. The condition is difficult to diagnose when complications ensue, but in spite of being highly lethal in the presence of complications, surgical therapy is the only chance of survival.

Resumen y Conclusiones

Hemos presentado el caso de una joven de 18 años de edad, retardada mental y sordomuda. El historial fue imposible de obtener. Presentó esta paciente con un abdomen agudo que progresó a una peritonitis franca. Laparotomía demostró cambios inflamatorios crónicos y severos de toda la pared del intestino delgado los cuales simulaban aquellos que se suelen ver con enteritis granulomatosa. La paciente falleció al séptimo día post-operatorio debido a perforación del intestino y aspiración de contenido gástrico. La autopsia demostró un tricofitobezoar en todo el intestino delgado con múltiples úlceras y perforaciones. Discutimos en este manuscrito el cuadro clínico y los factores diagnósticos principales, siendo factor clave un alto índice de sospecha. La condición es muy difícil de diagnosticar en especial cuando se desarrollan complicaciones, pero a pesar de su alto índice de mortalidad en presencia de éstas, la única oportunidad de sobrevida es con terapia quirúrgica.

Acknowledgment

The authors wish to express their gratitude to Dr. Eduardo A. Santiago Delpín from the University of Puerto Rico Medical School for his contributions during the preparation, writing and editing of this manuscript.

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FORO DE MEDICINA NUCLEAR

RETROSTERNAL GOITER

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David Pérez, MD

Case Summary

This was the first admission to the Veterans Administration Hospital of this 36-year old male who presented in November 1974 with a two month history of right shoulder pain, radiating to right arm, increased by movement of the extremity and associated with neck pain. A chest film done in another hospital showed displacement of the trachea toward the right side by a mass in the mediastinum. Repeated chest films and tomograms (Fig. 1) done at the Veterans Administration Hospital confirmed previous findings.

Neck examination revealed a palpable suprasternal mass on the left side that moved with deglutition.

A 24 hours radioiodine uptake was 68 percent. Scintiphotos and scan of the thyroid gland (^{131}I) revealed a deformity of the left lobe which was displaced laterally and had a concave inferior border. Concentration of the isotope was also noted in a

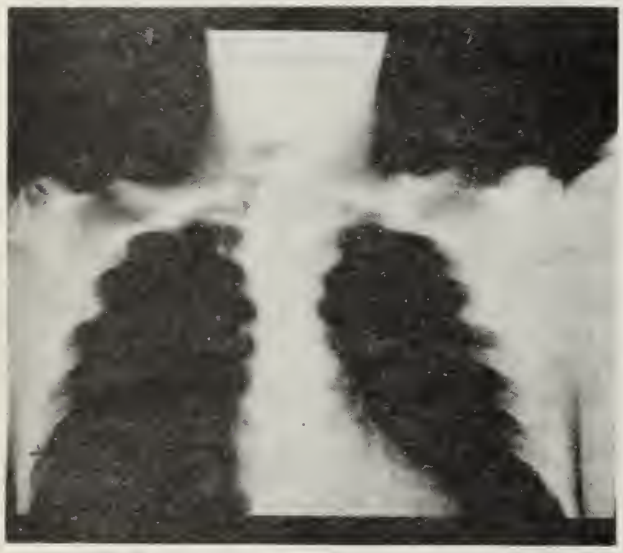


Fig. 1: *Tomogram of the chest.*

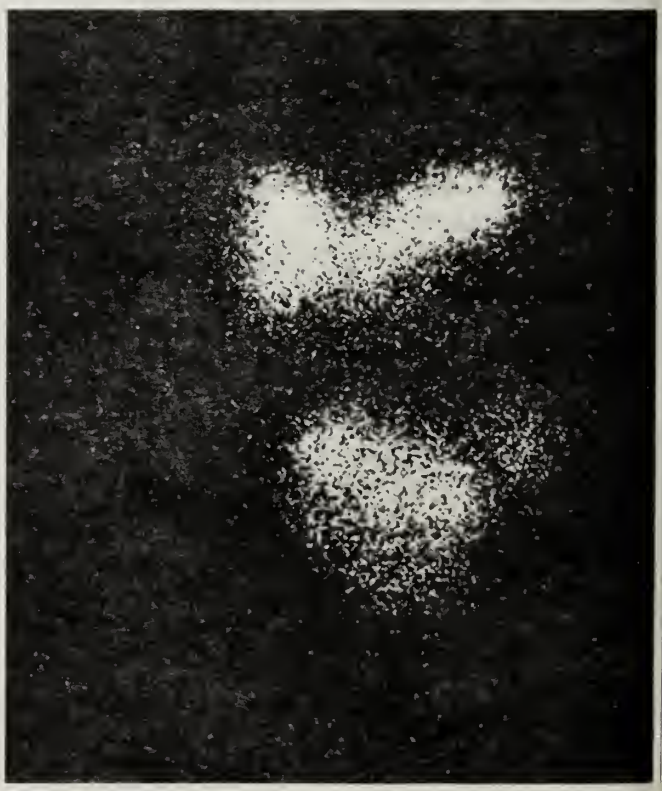


Fig. 2: *Scintiphoto of the thyroid gland.*

From the Nuclear Medicine and Surgical Services, Veterans Administration Hospital, San Juan, Puerto Rico.

separate region below the sternal notch which was separated into a larger and a smaller mass. This was reported as a retrosternal goiter with a multi-nodular gland in the neck (Fig. 2).

Surgical exploration of the neck revealed a retrosternal mass displacing the trachea and esophagus to the right. The pathologic report was of a mass of thyroid tissue weighing 85 gms. Histologic diagnosis was nodular goiter with degenerative changes.

The patient had an uneventful recovery after surgery and is now completely asymptomatic.

Discussion

Embryologically the thyroid gland is formed from evagination of the pharyngeal epithelium. Due to progressive midline descent, thyroid tissue may be found from the base of the tongue to the superior mediastinum and it can also migrate together with the cardiovascular structures (1).

Mediastinal thyroid tissue is usually located in the superior mediastinum and receives blood supply from thyroid vessels. Intra-thoracic goiters are almost always extensions of cervical goiters and they may produce displacement of the trachea, neck vein distension due to compression which account for symptoms of dyspnea, stridor, dysphagia and facial swelling. The mass usually moves with deglutition. Removal with cervical thyroidectomy is recommended (2).

Morphology of the gland can be determined by means of radioisotope scanning, following the oral administration of a tracer dose of iodide. Using ^{131}I which is preferred because it is organified within the thyroid tissue and it has a convenient half life of eight days, the study is performed within the next 24 hours (3).

^{99m} Technetium is also used as a thyroid scanning agent after intravenous administration. This isotope is not organified by the thyroid gland and its major advantage is reduced radiation dose to the patient due to lack of beta emissions. This isotope should not be used in the evaluation of sub-sternal goiter due to the high background activity.

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PROGNOSIS EN EL CANCER PULMONAR

No cabe duda en las mentes de los médicos y laicos del aumento en la incidencia y mortalidad por cáncer del pulmón. Durante los últimos 30 años, en que he dedicado mis esfuerzos orientados hacia la cirugía torácica y cardiovascular, he observado, como asi en otros sitios y por otros cirujanos, la declinación aguda en la incidencia de las enfermedades infecciosas del pulmón, incluyendo la tuberculosis, y ha ido "in crescendo" la incidencia y mortalidad por cáncer del pulmón.

Estudios experimentales, estudios étnicos y estudios documentados de incidencias y catástros en zonas industriales indican la estrecha relación de causa y efecto en la etio-patogenia del cáncer del pulmón.

Los resultados del tratamiento con diferentes métodos o combinaciones de métodos convienen en una sobrevida a 5 años o más, en un 7 por ciento a 8 por ciento. Aquí en Puerto Rico los resultados en el Hospital Municipal llega apenas a 1.5 por ciento y en el Auxilio Mutuo a un 3 por ciento como así también en el Hospital Universitario.

Cabe entonces la pregunta ¿por qué tan pobres resultados en el tratamiento del cáncer del pulmón? Revisando nuestra casuística personal encontramos algunas respuestas a esta pregunta:

Primero: Desde el punto anatómico el pulmón es uno de los pocos órganos con doble circulación (dos sistemas arteriales).

Segundo: Toda la sangre deberá pasar obligatoriamente a través de los capilares pulmonares.

Tercero: Ultimos estudios intravitales del sistema linfático han demostrado que solamente algunos segundos bastan para que un tinte inyectado subpleuramente aparezca en los ganglios nodiastinales. Sigue pues lógicamente pensar que la anatomo-fisiología pulmonar tan necesaria en la homeostasis resulta un arma de dos filos permitiendo la fácil diseminación de una neoplasia pulmonar, por esto vemos en un 30 a un 40 por ciento de los pacientes afectados por cáncer, metástasis síncronas que ya pueden ser macroscópicas o ya se hacen manifiestas, por ser micro-metástasis, desde meses o años seguidos a la resección pulmonar.

Cuarto: El prognóstico en cuanto a sobrevida de 5 años, tiene relación íntima con la oncología del tumor. Los mejores resultados los tenemos con tumores epidermoides maduros y los peores con anaplásticos e indiferenciados. Los adenocarcinomas, a pesar de su madurez tienen peor prognóstico que los epidermoides maduros. Los bronchoalveolares tienen dos formas de presentación:

Primera: La forma circunscripta de buen prognóstico y

Segunda: La forma diseminada, multicéntrica o pneumónica de peor prognóstico.

Los mal llamados adenomas bronquiales, los consideramos y tratamos como tumores malignos, ya que en los ganglios extirpados con el lóbulo o pulmón encontramos metástasis en alrededor de un 40 por ciento, y hemos visto morir pacientes por metástasis al hígado 13 y 14 años después de la resección pulmonar por carcinoide o por muco-epidermoide. Los cilindromas tienen una gran tendencia a recidivar cuando se originan en bronquio principal o los hemos visto con metástasis cuando se originan en traquea.

Por todo lo arriba expuesto llegamos a deducir que el tratamiento del cáncer del pulmón exige la consideración de muchos factores para poder tratarlo con un éxito relativamente aceptable:

Primero: *Considerar hallazgos clínicos (presencia de metástasis al drenaje linfático o a distancia, invasión a estructuras vitales, etc.*

Segundo: *La histopatología (los de células avenadas "oat-cell", anaplásticos de células gigantes) son totalmente inoperables y todo tratamiento resulta futil. Solamente un caso de célula avenada sobrevivió 9 años y dos casos de células gigantes pasaron los 4 años en los cientos de casos de cáncer de pulmón con los que hemos bregado en estos 30 años.*

Tercero: *La localización de la neoplasia habrá de considerarse en la determinación de tratamiento y prognóstico.*

I. Forma numular (Coin lesion) - Esta forma es operable. En 100 casos consecutivos el 65 por ciento resultaron lesiones benignas (tuberculomas, histoplasmomas, abscesos cerrados, quistes, hamartomas) el 45 por ciento resultaron neoplasias de los cuales 4 resultaron carcinoides periféricos y el resto carcinomas epidermoides, adenocarcinomas, scarcarcinom, indiferenciados, broncoalveolares.

A pesar de lo incipiente y bien delimitadas las lesiones y a pesar de no encontrarse metástasis linfáticas sería de esperar una sobrevida alta; digamos sobre un 70 por ciento a 80 por ciento. Sorprendentemente la sobrevida en estas lesiones tempranas apenas llegan a un 25 por ciento! a los 5 años. La muerte aún tempranamente, esto es, meses después de operados ocurre mayormente por carcinomatósis hematógena (hígado, sistema nervioso y oseo, suprarenales).

II. Forma paramediastímica - derecha- Mayormente epidermoide en fumadores, causa tempranamente obstrucción de vena cava superior. Los hemos tratado con cobalto preoperatorio seguido por excisión radical con resección parcial de cava superior. Resultados pobrísimo. Mortalidad dentro del primer año.

III. Forma paramediastinica izquierda - Se presentan con parálisis de frénico y o recurrente. Esta forma es incurable usando todos los métodos a nuestro alcance.

IV. Forma Subpleural - de difícil diagnóstico. Pacientes tratados mayormente desde el punto de vista ortopédico, neurológico, etc. de curso clínico larvado, lento; puede llegar de 3 a 3 1/2 anos terminando con dolores intratables del brazo. torax, Horner. Mayormente epidermoides en nuestros casos.

V. Syndrome de Pancoast - (parecido al anterior) - Diagnóstico puede hacerse un poco más pronto; destrucción de costilla o apófisis transversa. Los hemos tratado con Cobalto 60 preoperatoriamente seguido por resección de I-II-III-IV costillas y apófisis vertebrales con lópulo superior "en block". De 6 casos uno resultó adenocarcinoma - el resto epidermoide - Estos casos no sobrepasan, en nuestras manos, los 2 años.

VI. Tumor Excavado - Se confunde con lesión inflamatoria por lo general. Son carcinomas de crecimiento rápido anaplásicos o indiferenciados. Las resecciones amplias con pared que hemos hecho han tenido sobre vida corta, de 1 a 2 años.

VII. Forma Penumonítica - Broncoalveolares, indiferenciados - muestra crecimiento

en las venas pulmonares. Aún resecando pericardio y atriectomia izquierda parcial con venas pulmonares - 6 casos - los pacientes mueren tempranamente por metástasis hematógena.

VIII. Tumor Central o Hiliar - de fumadores - Síntomas tempranos. Si muy grande (4-5cm) cobalto preoperatorio seguido por resección. En su gran mayoría son epidermoides. Sobrevida variable.

IX. Tumoración gigante - Pseudo encapsulado. Algunos pacientes demuestran gran estado inmunológico; a pesar del tiempo y tamaño no se descubren metástasis a distancia. Son operables siendo mayormente epidermoides. Un solo caso resultó carcinoma-sarcoma que vive aún después de 6 años libre de metastasis.

Levantando el telón, la venda ante nuestros ojos aflojada, nos preocupa y horroriza el cuadro tan triste que presenta el carcinoma de pulmón. Parecería ahora decir que la nariz, según Panglos, se hizo para sostener las gafas o espejuelos si afirmo que hay que evitar la formación de un cáncer de pulmón.

Hablando ante el Colegio Médico Lucense en agosto de 1959 decía, cuando describía la historia natural del cáncer del pulmón, que nosotros, la raza humana, pasábamos cánceres que nuestro sistema de defensa podía eliminar hasta tanto los elementos carcinogenéticos a fuerza de persistencia lograban romper la barrera de defensa y entonces se hacía manifiesto el cáncer.

Cada vez que reviso mi casuística de cáncer de pulmón se reafirman en mí aquellos conceptos expuestos en 1959. Como colofón deseo repetir lo que algunos de ustedes han oído de mí:

I. Evitar el fumar, especialmente cigarrillos.

II. Evitar los tapones "de carros sugiriendo al gobierno, escuelas, negocios, etc." el escalonamiento en la entrada y salida de empleados, estudiantes, etc.

III. Hacer consciente al gobierno y empresas privadas la necesidad de un aire limpio, o lo más bajo en substancias productoras de cáncer.

David Rodríguez-Pérez, MD
V. A. Hospital
San Juan, Puerto Rico

HEW NEWS:

The Department of Health, Education, and Welfare today published final regulations permitting public and non-profit home health agencies to arrange with proprietary agencies for home health services under Medicare.

The home health agencies will be required to assume control and supervision of the services just as if they were provided by their own employees. Until now, public and non-profit home health agencies could arrange for services only with other public and non-profit organizations.

Medicare hospital insurance pays for up to 100 medically necessary home health visits in a benefit period. Also, medical insurance can pay for 100 home health visits in a year after the beneficiary has met the $60 yearly deductible.

The regulations take effect 30 days after today's publication in the Federal Register.

The basic premium paid by Medicare beneficiaries for their supplementary medical insurance coverage will increase from the present level of $6.70 a month to $7.20 a month for the 12-month period beginning next July.

The supplementary medical insurance program, also known as Part B, complements the basic hospital insurance part of Medicare by helping to pay physicians' bills and a wide variety of other medical expenses in and out of the hospital. The costs are shared by the participants and the Federal Government.

About 24.4 million persons will be enrolled in the supplementary medical insurance part of Medicare in the coming fiscal year, including 2.2 million disabled persons under 65.

HEW Secretary David Mathews said the law requires him to review in December the cost of the supplementary medical insurance program and to set a premium rate which, together with the Federal contribution, is estimated as sufficient to cover all expenditures that will be incurred in the 12 months beginning July 1, 1976.

The law also requires that any increase in the premium amount next July 1 must be limited to the percentage by which social security cash benefits increased in 1975.

"Social security benefits increased by 8 percent in June 1975," the Secretary said. "As a result, the medical insurance premium can increase by no more than 8 percent. The mathematics produces a premium rate rounded to $7.20 a month, effective July 1, 1976."

If there were not an 8 percent limit on the premium increase, rising medical costs would require an "actuarially adequate" premium of $10.70 a month, or $3.50 more than the premium that will actually be charged. The "actuarially adequate" premium represents a 50 percent share of the costs of aged participants.

The cost of the supplementary medical insurance program is expected to increase from about $4.7 billion to $5.7 billion in the following year, the Secretary said. The major factors are projected increase in physicians' fees recognized by Medicare, increases in the number of services rendered, a trend toward more expensive services, and an increase in the cost and use of hospital outpatient services.

Some Part B beneficiaries pay more than the basic premium because they enrolled late or becuse theya withdrew and then re-enrolled. Their premiums also will increase beginning July 1, 1976.

This will be the first increase in the medical insurance premium since July 1, 1974. Despite rising medical costs, the premium could not be increased on July 1, 1975, because of a technical error in the law. The error was corrected by legislation enacted by Congress in December 1975.

THE AMERICAN ASSOCIATION FOR CLINICAL IMMUNOLOGY AND ALLERGY will have its annual scientific and business meeting November 28-December 2, 1976, at Braniff Place Hotel, Tucson, Arizona.

Please notice that this is a change from previously announced dates and that other 1976 dates for this organization should be disregarded.

ARTICULOS A PUBLICARSE EN LA EDICION DE MARZO

1. Poisoning in Children - *Sidney Kaye, MSc., Phd*
2. Hipotiroidismo en Síndrome de Down. Informe de un caso y revisión de la literatura. - *A. Pêrez Comas, MD*
3. Surgery from a Practical Viewpoint - *Nathan Rifkinson, MD*
4. Is Monocular Testing in Presbyopes Useful? - *Manuel N. Miranda, MD*
5. Educación Médica Continuada - *Egidio S. Colón Rivera, MD*

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VOL. 68 Marzo 1976 No.3

Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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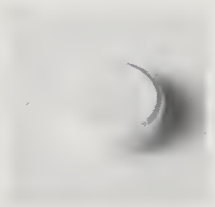
MAY 14 1976

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium® (diazepam) IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic anxiety states with associated depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Diuretics reduce blood pressure by blocking sodium retention to lower "effective" volume. But, the body's renal compensatory mechanisms are mobilized to promote sodium conservation, expand "effective" volume and reelevate blood pressure. Sustained control of "effective" volume is therefore essential to treatment. Hygroton blocks sodium retention longer than any other diuretic available.

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BRIEF SUMMARY

Indications: Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone; routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May be additive or potentiative of the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Usage in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in cord blood and breast milk. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis; dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia; purpura, photosensitivity, rash, urticaria, necrotizing angiitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg. (white, scored) and 50 mg. (aqua) in bottles of 100 and 1000; single-dose blister packs, boxes of 500; PAKs of 28 tablets, boxes of 6.

BOLETIN ASOCIACION MEDICA DE PUERTO RICO

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Volumen 68 Marzo 1976 Número 3

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Ascriptin,® an excellent analgesic, antipyretic, and anti-inflammatory, combined with codeine to give effective relief from severe pain with minimal aspirin-induced gastric distress.

Indication: As an analgesic for the relief of pain of all degrees of severity up to that which requires morphine.

Side Effects: Side effects are rare. Nausea, constipation and drowsiness may occur.

Warning — may be habit forming.

Usual Adult Dose: Ascriptin with Codeine No. 2 (¼ grain): Two tablets every 3 or 4 hrs. when necessary.

Ascriptin with Codeine No. 3 (½ grain): One or two tablets every 3 or 4 hrs. when necessary.

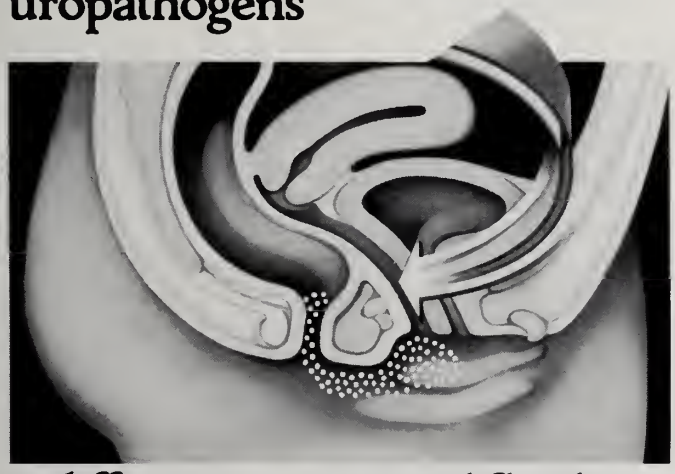
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SEPTRA®.
Does this urinary antibacterial discriminate in favor of women?





It eliminates most pathogenic enterobacteria from the bowel, a major source of reinfecting uropathogens



It diffuses into vaginal fluid, helping to keep the introitus free of uropathogens

The main route to reinfection in women with recurrent bladder infections can now be traced with precision.

Bacterial serotyping has confirmed the bowel as the ultimate reservoir of reinfecting uropathogens.[1-4] Periodic vaginal cultures have shown that virtually every recurrence is preceded by colonization of the vaginal introitus with *E coli* or other enterobacteria.[1] From the vaginal introitus, bacteria easily reach the bladder via the ascending route.

Unique pharmacokinetics make SEPTRA particularly well suited to block this route to reinfection in women.

During SEPTRA therapy, *E coli* and other enterobacteria usually disappear from the fecal flora.[5-8] So there are few, if any, pathogens left to recolonize the perineum. This change in fecal flora has rarely been associated with problems of diarrhea[7,8] or emergence of resistant strains.[5-8]

In addition, minimal inhibitory concentrations of trimethoprim for most strains of Enterobacteriaceae are similar to the levels found in vaginal fluid during therapy with SEPTRA.[9] In women with recurrent urinary tract infections, SEPTRA has been shown to eradicate enterobacteria from the vaginal introitus and help prevent recolonization with fecal pathogens.[1,9,10]

Artist's conception of route by which bacteria from bowel can enter urinary bladder.

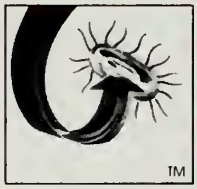
SEPTRA®

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazole

blocks the main route to reinfection in women with recurrent cystitis due to susceptible organisms

Note: Septra is contraindicated during pregnancy and the nursing period. See next page for prescribing information.



SEPTRA®

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazole

Effective in recurrent cystitis, pyelitis, and pyelonephritis due to susceptible organisms

- **effective against major urinary pathogens responsible for recurrent infections—*E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris, Proteus morganii***
- **double blockade of bacterial metabolism delays development of resistance *in vitro***
- **unlike most urinary antibacterials, SEPTRA has a convenient b.i.d. dosage schedule; reduces risk of missed doses**
- **available in tablets or cherry-flavored suspension**

INDICATIONS: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

CONTRAINDICATIONS: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

WARNINGS: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **At present, data are insufficient to recommend use in infants and children under 12.**

PRECAUTIONS: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

ADVERSE REACTIONS: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

DOSAGE: Not recommended for children under 12. Usual adult dosage: 2 tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

SUPPLIED: Tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

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POISONING IN CHILDREN

Sidney Kaye, MSc., Ph.D.

Poisoning is a serious problem all over the world resulting in many deaths. Exactly how many deaths occur no one knows. But it is in the many thousands in the United States of America and perhaps in the hundreds in Puerto Rico. It is then no wonder that the third week of March is now set aside in the United States and in Puerto Rico as "Poison Prevention Week", as a reminder to try to minimize the many potential dangers in our home and at work (1).

It is estimated (in the USA) that for children alone, at least 500,000 are taken each year to their Physician in a question of acute poisoning. Fortunately most of these children live. In these cases, survival is not the only consideration. The child may be left with a permanent disease, mental retardation or physical disconfiguration. It is in an effort to minimize these dangers that the following short resumé is offered.

Poisonings in children had been most frequent between the ages of 1 to 6. More children are killed in this age group than by diphtheria, polio, measles, whooping cough and all the other dreaded childhood diseases totaled together. But now that our youths are becoming more "involved", we must widen our interests.

Not since the "middle ages" has poisoning been such a problem as it is today. Todays problems, however, are for different reasons; suicides and accidental poisoning now are the more frequent manner of death. Can it be because of the "population explosion", or is it (more likely) the ever increasing number of effective drugs and household chemicals now available to us that work so well and are relatively inexpensive? It is therefore no surprise that they are found in almost every home and are part of the new "better living". But these can be dangerous when used carelessly or used for purposes other than intended.

All chemicals and drugs are potentially dangerous when in sight and reach of children. Many things in our home contain a "lethal time bomb" that could be triggered off by the tiny fingers of a normal curious child. Physician's children are not exempt. As a matter of fact they are even more exposed to the extra (professional) dangers of whatever is carelessly left around by the parent. This is in addition to what could be found in the kitchen, (especially in the pantry or under the kitchen sink). What you may find would shock you!

The cause and manner of death seems to vary with geographic area. Alcohol in adults and aspirin in children have been the number one killers in the United States for many years. Aspirin (for some unknown reason) has not been a very serious problem in Puerto Rico. Up until recently (1972), alcohol (3) has not been diagnosed as a very frequent cause of death. But in 1972, it was found to be the most frequent cause of death due to a poison overdose; and unfortunately, too many of your "youths" (within the last few years) are rapidly becoming involved with this number one drug problem (alcoholism) (3, 4).

Parathion and its derivatives had been our most frequent cause of death due to poisoning in Puerto Rico up until 1972. This is a highly effective insecticide; but is too toxic for home use. It's MLD (minimum lethal dose) for a 150 lb man is about 25 mg. This is a *mighty toxic* and potent agent; and there are laws governing its packaging and sale, but apparently these laws are not too easily enforced. This is obvious as shown by our previous data* for Puerto Rico (2, 3, 5).

For a while (1966-1972), the ever increasing abuse and drug overdose of heroin among our "restless"

From the Legal Medicine & Pharmacology School of Medicine, University of Puerto Rico.

Presented at the Puerto Rico Medical Association (Pediatric Section) and the American Academy of Pediatrics (Puerto Rico Chapter), 22nd. Annual Meeting, February 8-12, 1975, San Juan, Puerto Rico.

** - Cases referred to the Institute of Legal-Medicine for autopsy.*

youths seemed destined to become our number one killer. Somehow this did not happen. In 1972 heroin overdose deaths began to decline, and alcohol overtook parathion as the most frequent cause of death due to poisoning (3).

Common Sense Measures to Prevent (or Minimize) Poisoning

1) Keep all drugs, pesticides, chemicals, cleansers, etc., out of the sight and reach of children. (What is in sight they try to reach). Under the kitchen sink is a favorite space for "cleaners and corrosives" (thoughtless mothers).

2) Do not store any non-edible products on shelves used for storing food.

3) Keep all products in their *original* containers and do not *ever* transfer to an unlabeled container. Kerosene in a "cola" or milk bottle could be "murder" by sheer carelessness.

4) Discard all old medicine. The medicine cabinet is already too full; and since medicine isn't whiskey, "it does not improve with age".

5) When medicines are discarded, destroy them or flush them down the comode. Do not throw them where they can be reached by children or pets. (Trash cans are a favorite spot for kids to play).

6) When giving flavored and/or colored medicine to children, *NEVER* call it candy; he may believe you and eat some when you are not around.

7) Read labels before using; use as prescribed; do not guess, or be your own doctor; never take medicine in the dark (sounds silly, but this is often ignored).

Use *tight* closure (type) medicine bottles. If somehow they do get hold of it (as it will happen), at least make it tough or impossible for children to open.

9) Regard all pesticides as dangerous and treat as such. They were made to kill – but not us. Avoid the *very* potent types; the less potent are also effective insecticides.

10) The unavailability of "very" toxic agents at home may make the important difference at that "frantic" moment of suicidal urge. At least, let us not make it too easy or too available for the teenagers.

11) Now that we know that alcohol is a very serious problem in drug abuse, perhaps a greater effort must be made to "educate" our youths in the art of responsible drinking and thus try to minimize its role in tragedy.

Poison Control Centers

When a poisoning occurs (as it will), central facilities must be available in every district to assist in making a rapid, reliable evaluation. Diagnosis is not always easy.

Each district hospital must expand their Poison Control Center facilities to include information, treatment and simple rapid testing – at least for the more common (frequent) poisoning occurring in their district. Time and experience will expand their expertise to include the less common ones.

A district Poison Control Center is a vital hub for information, diagnosis and treatment which can be set into operation with a minimum of money and effort – but it does require an interest and enthusiasm to do so.

The first such center was established in the United States about 20 years ago.

In the U. S. A. and Europe there are now many such centers, most of which operate in hospitals. A Poison Control Center may begin modestly, expanding as experience and need increases.

In addition to the card file on local available products, a poison information center should purchase a few standard reference books on toxicology (6, 8, 9, 10, 11, 12, 13, 14, 15). Both the file and the references will grow as new problems are brought up.

Poison Control Centers have been designated in Río Piedras, Ponce, Mayagüez, Aguadilla, Arecibo, and Fajardo Medical Centers by the Secretary of Health and by the Medical Directors of each District Hospital to serve their area. It is hoped that these Poison Control Centers may be of service to you in time of need (for advice or assistance). The address and telephone numbers of these centers are listed below:

Poison Control Centers

Health Department, Commonwealth of Puerto Rico

INFORMATION AND TREATMENT

CONSULT YOUR NEAREST POISON CONTROL CENTER FOR INFORMATION AND FOR FURTHER SUPPORT (IF NECESSARY)

1. (a) Medical Center - Río Piedras
   Tel. 763-7272 (Ext. 45) or
   Tel. 764-3515 (Direct) - Internist in charge; according to duty roster.
   (b) Hospital Presbiteriano - Tel. 723-4111

2. Arecibo District Hospital
   Dr. Ramón Vélez Arce, or Tel. 878-3535 - Physician in charge; according to duty roster.

3. Ponce District Hospital
   Tel. 842-8364 or
   Tel. 844-2080 - Dr. Hermes Flores, Jefe

4. Fajardo District Hospital
   Tel. 863-0505 - Dr. Tomás López Colón, Jefe

5. Mayagüez Medical Center
   Tel. 832-8686 - Dr. Themistocles J. Ramírez Echevarría, Jefe

6. For information only: School of Pharmacy (U. P. R.), Río Piedras Campus Library
   Tel. 764-0000 Ext. 2484 or 2480 - Lic. Julia G. de Andreu, Director - Lic. Felícita Rojas, Lic. Glenda Sobrino

7. Coordinator
   Tel. 765-0615 - Dr. Sidney Kaye, School of Medicine, U. P. R.

Evaluation and Diagnosis

It is a moment of decision when a frantic mother rushes into the emergency room with her child:

"My baby just swallowed a poison".

Diagnosis is not always easy. Which poison is it (if any); how toxic is it; where is the container, does it have a label; what does it look like, (liquid, solid, color, odor); are these characteristic or typical of anything we recognize?

How is the patient? Typical signs or symptoms, or any suggestions could be a great help. Speed is important!

General Symptoms and Signs (6, 7)

Symptoms and signs are the effects, stated or observed, produced by the action of a particular poison on the physiologic functions of the body. These effects are frequently quite characteristic, specially in the absence of other possible causes. For example, coma may suggest barbiturates and would rule out strychnine. *Many diseases*, however, produce symptoms similar to those caused by poisons and special care is urged in the differential diagnosis.

A partial listing of some of these common *symptoms* and *signs* follows; however, these symptoms are not infallible. Confirmation of the suspected poison by history and circumstances and by simple, rapid, reliable methods of identification would still be indicated (6, 7, 8).

VOMITING & G. T. UPSET: Heavy metal salts; alcohols; corrosive acids and alkalies; halogens; cantharides, croton oil; yellow phosphorus; phenols; muscarine; digitalis; fluoride; *parathion* and other organic phosphate esters; and many poisonous plants, etc.

CONVULSIONS: Strychnine, parathion, and other organic phosphate esters; amphetamines, ammonium salts, aspidium, brucine, camphor, saponin, caffeine, aconitine, picrotoxin, cyanides, chlorinated hydrocarbons, lead, barium, diamox, belladonna, stramonium, and other atropine-like compounds. Stimulants or analeptics.

COMA: Alcohols, opium, morphine, heroin, barbiturates, tranquilizers, antihistamines, chloral hydrate, sulfonal, paraldehyde, chloroform, ether, salicylates, carbon monoxide, carbon dioxide, nicotine, phenols, hydrogen sulfide, lead, bromides, benzene, xylene, organic solvents, and other depressants.

GENERAL OR PARTIAL PARALYSIS: Cyanide, carbon monoxide, carbon dioxide, botulism, alcohol, nicotine, aconitine, barium, curare, mercury, arsenic, lead, and DDT.

CONSTRICTION OF PUPILS: Opium, heroin, morphine and derivatives, parathion and other organic phosphate derivatives, physostigmine, pilocarpine, muscarine, other parasympathomimetic drugs, ergot.

DILATATION OF PUPILS: Belladonna group (atropine), Datura strammonium, sympathomimetic group-epinephrine, amphetamines, cocaine.

Blood Changes

DECREASED COAGULABILITY: Dicumarol, (warfarin), coumadin, heparin, benzene, phosphorus, fluorides, carbon monoxide.

BASOPHILIC STIPPLING: Lead, arsenic, gold.

CHERRY RED BLOOD: Carbon monoxide (carboxyhemoglobin), cyanide.

DARK RED BLOOD: Nicotine.

CHOCOLATE BLOOD (METHEMOGLOBIN): Aniline and nitro derivatives, acetanilid, nitrobenzene, plasmochin, sulfonal, chlorates, nitrites, sulfa drugs, methylene blue (high concentration), phenacetin.

AGGLUTININS: Ricin, croton, abrin, poisonous mushrooms, some snake venens.

Cardiovascular Changes

BRADYCARDIA: Barium, aconite, digitalis, muscarine, Eserine, pilocarpine, quinine, quinidine, parasympathomimetic drugs.

TACHYCARDIA: Anesthetics in general, amphetamine, atropine (belladonna group), cocaine, ephedrine, epinephrine (group).

HYPOTENSION: Arsenic, barbiturates, aspirin, phenacetin, meprobamate, phenothrazines, amidopyrine, chloroform, muscarine, nitrites, arsine, Doriden, librium, quinine, iron salts, Endrin, Aldrin, Dieldrin.

CAPILLARY PERMEABILITY (HEMORRHAGE): Arsenic, benzene, gold, corrosives, iodides, antimony, Dicumarol, sulfa drugs, thiouracil, Dilantin, some snake venens, histamine, (H)-like sustances, aspirin.

AURICULAR FIBRILLATION: Fluoroacetate (1080), digitalis, red squill, Metrazol, nitroglycerin, quinine, carbon monoxide.

FLUSHING: Acrolein, amyl nitrite, aniline, aspirin, amphetamine, atropine, belladonna (group), camphor, codeine, curare, ephedrine, alcohol, ethyl bromide, gasoline, gelsemine, mercury, nitroglycerine, paraldehyde, santonin, scopolamine, red squill.

Disturbed Vision

PURPLE YELLOW VISION: Digitalis, marihuana, santonin, aspidium.

BLURRED VISION: Parathion, belladonna (atropine) group, especially atropine, solanine, methyl alcohol, ethyl alcohol, TEPP, HETP, DFT, ergot, thallium, carbon tetrachloride.

PARTIAL OR TOTAL BLINDNESS: Methyl alcohol, formic acid, methyl chloride, methyl bromide, aspidium, solanine.

Other Changes

ACIDOSIS: Mercuric chloride, sulfa drugs, aspirin, salicylates, methyl alcohol, oil of wintergreen, opium, morphine, ethylene glycol, oxalic acid, isopropyl alcohol, acetone.

ALOPECIA (loss of hair): Thallium, arsenic, alkali sulfides, radium, x-ray, ergot.

BUZZING IN EARS (TINNITUS): Salicylates, quinine, streptomycin, camphor, ergot, methyl arsenic.

COLITIS: Mercuric chloride, arsenic.

DRY MOUTH: Belladonna group, especially atropine, morphine, Benadryl, ephedrine.

INCREASED BODY TEMPERATURE: Dinitrophenols, toxaphene, amphetamine, arsenicals, atropine, camphor, cocaine, Thyroxin, Boric acid, Doriden.

LOWER BODY TEMPERATURE: Quinine, acetanilid, salicylates, aconite, chloral, nitrites, morphine, ether, chloroform, barbiturates, all central nervous system depressants.

INCREASED SENSITIVITY TO SOUND, TOUCH, HEARING: (Tingling of skin): Strychnine.

INCREASED SWEATING: Muscarine, pilocarpine, arecoline, dieldrin, parathion, DFP, HETP, TEPP, morphine, mercuric chloride, alcohols, insulin, nitrites, ammonia, arsenic, aspirin, salicylates, bismuth, fluoride, physostigmine, parasympathomimetics.

COLOR OF THE SKIN: Pink: Carbon monoxide; Yellow: Atrabine; Brown: Methemoglobinemia; Flushed face: Atropine group.

ABNORMAL COLORING OF THE URINE: Dark green: Phenol, salol, resorcinol; Brown or Black: Pyrogallol, antipyrene, trional; Yellow: Picric acid, quinacrine; Orange: Azogantrisin, pyridium; Blue-green: Doan's kidney pills, phenols.

DISCOLORATION (BLACK) OF GUMS: Lead, mercury, bismuth (usually chronic poisoning). "Burtonian Lines".

UNUSUAL DISTINCT ODOR OF TISSUES: Phenols, creosote, chloroform, H_2S, CS_2, ether, alcohol, crude opium, paraldehyde, and many others.

Garlic odor - phosphorus, arsenic, parathion (onions)
Bitter almonds - cyanides
Shoe polish - nitrobenzene
Violets - turpentine in urine
Pears - chloral hydrate

LIVER DAMAGE: Amanita phalloides, carbon tetrachloride, chloroform, chlorates, carbon disulfide, chromates, phosphorus (yellow).

KIDNEY DAMAGE: Alloxan, amanita phalloides, acetic acid, aloe, boric acid (borates), carbon tetrachloride, castor oil, chlorates, chromates, phenol, ethylene glycol, ferric chloride, fluorides, fava bean, formaldehyde, mercury salts, oxalic acid (oxalates), potassium permanganate, phenols, phosphorus (yellow), picric acid.

For further reliable confirmation it is advisable to have a quick, positive, presumptive test on the patient's blood, urine, or vomitus for whatever toxic agent is suspected. Many of these tests could be performed with confidence by the laboratory technician or by the attending physician with readily available simple equipment. Just because a test is simple and rapid does not imply that it is not reliable.

Suggested, presumptive tests (6, 18), when done in parallel with a positive control and a negative blank, are *reliable, sensitive*, and simple, and they require *little or no equipment.* They are especially rapid, and treatment can be continued with more confidence.

The following cases are examples of when a "quickie" test (8) could make a great contribution.

1. Three children were playing doctor, nurse and patient with *aspirin.* Only one has immediate symptoms. Did all three take the aspirin? Do you lavage all three?

2. A child with gastroenteritis with green-blue vomitus was sent home to rest. He was diagnosed and followed over the telephone. He died the next day. (Paris green; *arsenic).*

3. A child was seen with a strange, weird look and twisted neck and tongue. These are the side effects of *phenothiazine;* withdrawal of the drug was all that was necessary in many cases.

4. A sleeping child did not respond to attempts to awaken him. His mother secretly gave *pentobarbital* to keep the child from crying.

5. A child was "sleeping" in the back seat of an air-conditioned automobile. At the destination, which fortunately was near, his older brother staggered out and then feel unconscious *(carbon monoxide).*

6. A threat to commit suicide with aspirin was made over the telephone. The patient was found unconscious. A rapid test with ferric chloride on urine was negative, and a negative test is exclusive for aspirin. On a hunch, tests for alcohol were quickly made and were positive for large amounts of *ethanol,* directing the course of treatment.

7. *Parathion* is an excellent insecticide. It kills everything because it is extremely toxic, and it is very inexpensive. Therefore, it is no surprise that it is found in so many homes. It is the foremost "killer" in many areas of Latin America. Atropine is the specific antidote and can be life-saving if the diagnosis is made on time.

8. A "wet brain" of a child at autopsy initiated a field survey in the child's town. The urine of other children was positive for coproporphyrins. It was then easy to determine the source: Careless melting of *lead* plates from old batteries in a garage. Unfortunately two died before this was discovered and corrected.

9. A child gulped down a liquid that he found in a soft drink bottle. A rapid test for *kerosene* was positive and this alerted the attending physician to take all precautions to prevent aspiration into the lungs and to minimize possibility of pneumonia. The child survived.

Summary

To permit poisoning to occur so frequently and so easily, is senseless. Every effort must be made to prevent it from happening in the first place.

Parathion and alcohol poisoning continue to be the most frequent killer in Puerto Rico. We need laws (that are workable) to regulate its responsible use.

If a poisoning does occur (as it will), facilities must be made readily available to allow for a rapid and reliable diagnosis so that proper treatment may be given with more confidence and certainty. To this end each District Hospital must expand their Poison Control Center facilities to more easily assist in the diagnosis and possible treatment of poisoning. Rapid, simple, reliable presumptive tests for (at least) some of the more common poisons are now available to *all* hospitals and clinics.

It is sad to see the *increasing* number of deaths occurring each year due to ethyl alcohol over dose; it would be shameful if greater efforts *(somehow)* are not made to try to offset this trend, at least for our future generations.

Resumen

La frecuencia con que ocurren casos de envenenamiento no tiene razón de ser. Es esencial dirigir todos los esfuerzos de prevención disponibles para eliminar o al menos disminuir la magnitud del problema.

El Paratión y el alcohol siguen siendo las causas principales de muerte por intoxicación en Puerto Rico. La legislación existente, aparentemente, no ha sido efectiva en regular la venta y uso responsable de estos productos.

Para responder efectivamente con casos de intoxicación, tienen que existir facilidades que permitan llegar a un diagnóstico rápido y confiable y establecer un plan de tratamiento adecuado.

Métodos rápidos, sencillos y confiables para determinar por lo menos los venenos más comunes están disponibles en el presente en todos los hospitales y clínicas. Los Hospitales de Distrito necesitan expandir los servicios de sus Centros de Control de Envenenamiento para aumentar su efectividad en el diagnóstico y tratamiento de estos casos.

Es causa de gran preocupación la seriedad del problema del mal uso del alcohol y el creciente aumento en muertes por sobredosis de alcohol; y especialmente el creciente aumento donde están envueltos nuestros jóvenes.

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HIPOTIROIDISMO EN SUJETOS CON SINDROME DE DOWN.

Informe de un Caso y Revisión de la Literatura

A. Pérez Comas, MD

Marañón, Díaz y Mendizabal informaron en 1951 de un sujeto afecto de síndrome de Down e hipotiroidismo (1). Posteriormente, se han reportado 15 casos adicionales, destacando trastornos tiroideos de tipo autoinmune asociados a trisomía 21 (2-14). Se trata de una combinación rara, que entraña dificultad diagnóstica debido a las características de ambas condiciones.

En esta comunicación presentamos los hallazgos de un joven con ambas condiciones, quien fuera evaluado en nuestro consultorio.

Informe del Caso

R. G. P., varón nacido a término en 1950, tras un embarazo no complicado, de una madre de 27 años de edad y un padre, no consanguíneo, de 28 años de edad. Presentó un peso de 8 1/2 libras y una longitud de 21 pulgadas, destacando lengua algo grande, poco apetito y un estreñimiento pertinaz desde los primeros días de vida. A los 24 días de edad tuvo bronquitis, de la cual recuperó prontamente. A partir de los 5 meses la madre le notó la piel reseca. Se volteó a los 6 meses, sentó y gateó al año, parándose al año y medio y caminando solo a los 3 años. El primer diente brotó a los 6 meses.

Fue evaluado por múltiples médicos para determinar la causa de su retardo motor y del habla, y, a los 3 años fue evaluado por un médico de la localidad, quien hizo el diagnóstico clínico de hipotiroidismo, comenzándole terapia con tiroglobulina gr III por día. Continuó con dicha terapia, desapareciéndole el estreñimiento, aumentándole el apetito y logrando un desarrollo hasta varón adulto; con un lenguaje algo escaso, pero que le permite comunicarse, retardo mental moderado, con un desarrollo motor que le permite realizar su vida diaria y ayudar en algunas tareas simples de la casa.

En 1972 presentó un mareo con pérdida de conocimiento, palidez generalizada, sudoración fría. Se le hizo una tolerancia de glucosa oral de 6 horas, la cual no fue diagnóstica. Al mes y medio repitió la crisis, pero mejoró rápidamente con comida y no perdió el conocimiento. Debido a ello fuímos consultados.

Su examen físico (fig. 1) mostró un sujeto adulto bien nutrido y bien desarrollado, con un peso de 120 lbs., estatura de 60.5 pulgadas, cara con caracteres faciales mongoloides y retardo mental. Presentaba inclinación palpebral mongoloide, paladar ojival, orejas pequeñas, ligera micrognatia, boca entreabierta y cuello algo corto. La tiroides era palpable de un tamaño aproximado de media vez sobre el tamaño normal, estando bien delimitada, firme y algo gomosa al tacto. Presentaba además, los siguientes caracteres dermatoglíficos: surco de simio bilateral, incompleto en la mano derecha y com-



Fig. 1: *Sujeto adulto con caracteres del Síndrome de Down.*

De la Sección de Endocrinología Pediátrica y Genética Médica, Hospital Dr. R. E. Betances, Centro Médico de Mayagüez.

pleto en la izquierda, clinodactilia bilateral con hipoplasia de un surco en dicho dedo, bucle cubital en ambos índices, ángulo atd derecho de 80° y arco tibial en el área halucal derecha. El "dermatograma para síndrome de Down" (15) (figura 2), fue positivo.

Los estudios de laboratorio mostraron un cariotipo de 47, XY +21 (fig. 3), es decir trisomía 21 simple en un varón. La captación de radioiodo, una vez descontinuada la terapia con tiroglobulina, fue baja: 2.7 por ciento a las 2 horas y 2.5 por ciento a las 24 horas, no respondiendo a estimulación con tirotrofina exógena. No se hizo gamagrama de tiroides debido a la captación muy baja de radioiodo. El T-4 por radioensayo al descontinuar las medicinas fue de 0 ug$T4_I$ por ciento (normal 3.1-7). Los anticuerpos a tiroides fueron positivos a una dilución de 1:25.

El paciente continua con su terapia de tiroglobulina gr. III diario, una dieta de 1,500 calorías con 3 comidas y 3 meriendas. No ha vuelto a tener mareos, presentando una actividad normal para sus limitaciones.

Su historial familiar en tres generaciones no muestra consanguineidad. Como datos de importancia, destaca en su familia la presencia de un primo hermano (paterno) con trisomía 21 simple, varias primas maternas diabéticas, y una tía paterna y una prima materna hipertiroideas.

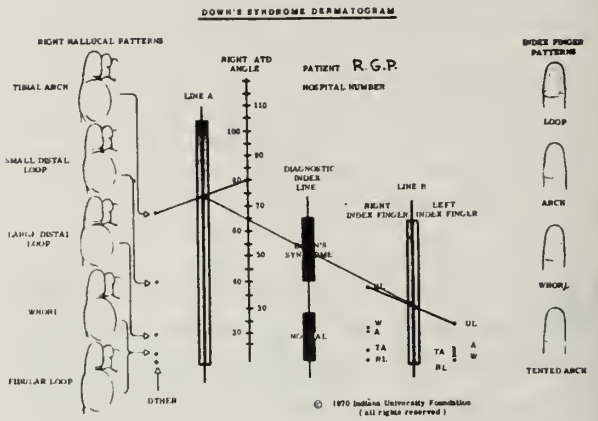


Fig. 2: *Dermatograma para Síndrome de Down positivo. Los caracteres dermatoglíficos confirman el diagnóstico presuntivo.*

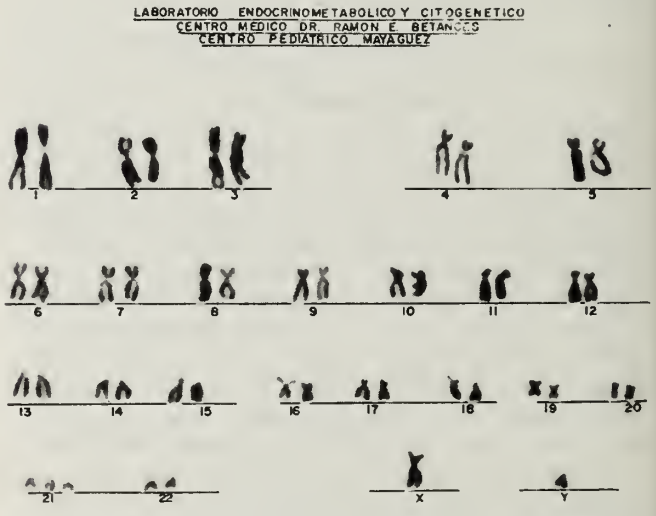


Fig. 3: *Cariotipo del sujeto que muestra Trisomía 21 simple. (47, XY, +G).*

Discusión

Durante muchos años los pacientes afectos de hipotiroidismo congénito (cretinismo) y el síndrome de Down han sido confundidos en el diagnóstico. Debido a algunos de los signos y síntomas del síndrome de Down (protrusión de lengua) hipoactividad, laxitud de extremidades, lividece, retraso pondoestatural y psicomotor, etc.), muchos pacientes han recibido terapia con preparaciones tiroideas, sin existir patología tiroidea alguna.

Para añadir más confusión, varios autores han encontrado sujetos afectos de ambas condiciones a la vez. Marañón y colaboradores (1), en 1951, informaron el primer caso de un niño mongoloide con hipotiroidismo, quien además presentaba pubertad precoz. La asociación de ambas condiciones es rara, habiéndose observado posteriormente en 17 casos, incluyendo el nuestro (1-14).

Destaca la incidencia elevada de anomalías tiroideas de probable origen autoinmune con anticuerpos a tiroides positivos. Doce de los diecisiete casos presentan hipotiroidismo adquirido (Tabla I), cuatro son probablemente hipotiroideos congénitos y en uno no hay datos exactos. Ocho de diez pacientes presentaron anticuerpos positivos y tres de nueve madres también los tenían positivos.

Diversos autores han encontrado una mayor incidencia de anticuerpos antiroides en sujetos con síndrome de Down (16, 17) y en sus madres (17-21). Wren y colaboradores, por el contrario, no encontraron un aumento en la incidencia de anticuerpos positivos en sus pacientes con trisomía 21, ni en sus madres (22).

El que la incidencia de anticuerpos en tiroides positivos sea mayor en sujetos afectos del síndrome de Down, y en sus familiares hacen pensar que la enfermedad autoinmune ejerza algún papel en la etiología de la trisomía. Este hecho, consideramos, debe ser estudiado más a fondo.

TABLA I
CASOS REPORTADO DE SINDROME DE DOWN ASOCIADO A HIPOTIROIDISMO

	PACIENTES					MADRE	
Referencia	Edad	Sexo	Cariotipo	Tipo Hipotiroidismo	Antic. Tiroides	Edad (*)	Antic. Tiroides
1. Marañón y colabs. (1)	12	M	-	?	-	40	-
2. Talbot y colabs. (2)	10/12	F	-	congénito (probable)	-	-	-
3. Esen y Mautner (3)	6	F	-	adquirido	-	19	-
4. Hubble (4)	5 6/12	F	47, XX, G+	adquirido	-	-	-
5. Hagles y colabs. (5)	13 6/12	F	-	adquirido	-	30	-
6. Pabst y colabs. (6)	8	F	47, XX, G+	adquirido	positivos	41	positivos
7. Matsaniotis y colabs. y colabs. (7)	6	M	47, XY, G+	adquirido	-	30	ausente
8. Harris y Koutsoulieris (8)	3 10/12	F	47, XX, G+	adquirido	positivos	27	ausente
9. Daniel y Simon (9)	17	M	47, XY, G+	congénito (?)	-	49	-
10. Litman (10)	1 1/12	M	47, XY, G+	adquirido	-	38	-
11. Lunde (11)	9 6/12	F	47, XX, G+	adquirido	positivos	46	positivos
12. Aarsgog (12)	1 3/12	F	47, XX, G+	adquirido	positivos	42	positivos
13. Williams y colabs. (13) (1)	17 6/12	M	47, XY, G+	adquirido	positivos	23	ausente
14. Williams y colabs. (2)	14	M	47, XY, G+	adquirido	positivos	25	ausente
15. Williams y colabs. (3)	3 6/12	M	47, XY, G+	congénito	positivos	25	ausente
16. Costin y colabs. (14)	8	F	47, XY, G+	adquirido	positivos	?	?
17. Pérez Comas	22	M	47, XY, G+	congénito (?)	positivos	27	ausente

-- *No hay datos* + Positivo M Masculino F Femenina * Al nacer el niño

Diversas condiciones endocrinas son de probable origen autoinmune y en ocasiones se encuentran presentes varias de ellas en un mismo individuo. Dicha etiología ha sido postulada en casos de insuficiencia adrenal, tiroiditis crónica de Hashimoto, hipotiroidismo primario, tirotoxicosis, hipoparatiroidismo idiopático, y algunos casos de diabetes mellitus (24, 25). Nosotros hemos observado una elevada incidencia de enfermedades de tiroides en sujetos diabéticos, y en sus familiares.

Resumen

El hipotiroidismo asociado a trisomía 21 es una condición extremadamente rara. Esta comunicación informa de un sujeto varón de 22 años que presenta ambas condiciones, representando el caso número 17 reportado en la literatura mundial. La combinación de ambas condiciones presenta dificultad diagnóstica.

Summary

Downs syndrome associated with congenital or acquired hypothyroidism is a rare condition. This paper presents the 17th case of the literature where both conditions are present in the same individual. Our case is a 22 year old male patient in whom the diagnosis of hypothyroidism was made at 3 years of age, and of Downs syndrome at 20 years of age. A review of the literature is made and the probable relationship between Down syndrome and autoimmune disease is mentioned.

Reconocimiento

Agradecemos al Dr. J. Ramírez Ledesma los estudios de

captación de radioiodo y el haber diagnosticado al paciente a los 3 años de edad, al Dr. Moisés Rivera Cordero el referirnos el paciente a los 20 años de edad, al Departamento de Fotografía del Centro Médico de Mayagüez el material fotográfico y a la Sra. Mirna Nazario la excelente labor secretarial.

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NEUROSURGERY FROM A PRACTICAL VIEWPOINT

Nathan Rifkinson, MD

At a meeting of the Royal Society of Surgeons in London, in the middle of the last century, the doctors present were electrified by the report of the first successful removal of a brain tumor. Up until that time, such attempts ended in the death of the patient.

There were many surgeons who knew how to open the skull in one way or another, but once inside the cranium they had no idea what to do.

Little was then known about functional localization in the brain, about how to deal with brain swelling or hemorrhage or how to prevent subsequent infection.

So this special day – listening to the exciting presentation by one of their colleagues, marked the beginning of a new surge of courage for many.

The news of this accomplishment spread fast throughout England, and wives of some of the doctors at their afternoon teas would boast that their John or Vincent were planning to operate on a brain tumor. Spurred on by their wives ambitions and dreams of fame, surgeons reported doing several hundred intracranial operations in the next ten years. But the results, as before, were a total disaster, so that in the succeeding decades there was a decreasing number of surgeons attempting this hazardous surgery – and by the end of the century, only a handful of men in the entire world, had the courage and the intense interest to continue in this most difficult, fascinating field.

The main reason for this difficulty lay in the fact that intracranial tumors are enclosed within a rigid bony case and cannot be palpated like tumors in other parts of the body. Detection of a brain neoplasm had to depend on other methods.

At that time, little else was known of brain function except that the cerebral hemispheres controlled the contralateral parts of the body. No one knew where to enter the skull with any degree of accuracy, and in a number of cases the skull was frequently opened on the wrong side.

But as the years of neurophysiological experimentation went by, the motor strip was discovered, the visual tracts were mapped out, as well as the various nuclei of the brain and brainstem, so that accuracy in opening the skull at or near the tumor site at the turn of the century was about 50 - 60 percent.

In spite of the greater accuracy in tumor localization, the death rate was still appalingly high because many of the problems peculiar to this type of surgery were still unsolved.

This was the insecure state of neurosurgery until in the early part of this century, Dr. Harvey Cushing called for a meeting of the remaining handful of men who alone in the entire world retained a consuming interest in brain surgery. They discussed the overwhelming problems which beset them, and it was agreed that those who wished to do neurosurgery, must give up all other type of work and devote their entire lives to this specialty – because of its complexity and its time-consuming demands.

Each of these men left the meeting inspired; left to return to his own area of work with lofty ideas and with renewed courage.

There were no textbooks of reference for guidance. Each brain operation was a new adventure. Each surgeon in his own way developed different approaches entering the different areas of the head, and at subsequent scientific meetings each listened to the merits of the others' methods and varied his own accordingly.

These wonderful pioneers frequently developed unusual surgical skill. Operations were interminably long frequently lasting ten or more hours. But this was of little concern to these courageous men. Some of these operations were technically brilliant and the surgeon would watch with intense elation as his patient slowly regained consciousness and became more alert day by day. But only too frequently by the fourth or fifth day, the temperature would rise, the patient become restless and slowly lapse into coma and die due to overwhelming meningitis.

Techniques were revised. Operating rooms scrubbed, gowns and instruments and sutures doubly sterilized in attempts to prevent this dreaded complication. Time for scrubbing of the hands and arms before surgery was lengthened to ten minutes and each neurosurgeon

developed his own routine which he made his assistants go through.

The man I started my neurosurgical training with, Dr. Ernest Sachs, Professor of Neurological Surgery at Washington University School of Medicine in Saint Louis, developed the following stringent routine:

After vigorous scrubbing of hands and nails and arms above the elbows for ten minutes with sterile green soap, we had to immerse our arms almost to the shoulders in 70 percent alcohol placed in deep sleeve-like metal containers. Next, in similar containers we immersed our arms in potassium permanganate up to our armpits, then we had to soak our arms in a lye solution which stung the skin sharply but also removed the dye. The fingertips were then immersed in caustic powder which was removed by dipping in a special chemical, after which we stained our hands in 2 percent iodine which we washed off in alcohol. If at the end of this procedure any spots of the purple dye remained anywhere on the skin, the entire routine starting with the potassium permanganate, had to be repeated.

Some of the residents developed eczematous, itchy rashes over their hands and arms and were kept from the operating room for weeks. In some the skin became so sensitive, that they were compelled to go into other fields.

Because of the almost insurmountable problems that confronted neurosurgery at the beginning of this century, very few young men were attracted to this specialty. The mortality rate was great, the morbidity high, and the reputation of the specialty and those that practiced it was quite discouraging.

Just what were those problems?

First, there was the great incidence of infection. Meningitis as a complication of intracranial surgery was extremely common. There were no antibiotics, and one had to depend on meticulous technique in the operating room and the natural resistance of the patient to infection. For as previously stated, many a brilliant operation ended in disaster because of this dread complication.

As an illustration of how helpless physicians were then in the face of meningitis, I wish to recount the tragedy of the only daughter of Dr. Ernest Sachs. She was twelve years of age when she developed meningitis. Treatment then consisted of fluids and antipyretics, and after weeks of becoming better and worse the girl slowly lapsed into a coma. Dr. Sachs was beside himself in grief. He frantically called his colleagues in Boston, and he was advised to follow the only treatment then known for this complication. So strong-minded was Dr. Sachs and so imbued with his own potential, that he chose himself as the surgeon to operate on his own child. He did a laminectomy in the lumbar region and found the dura to be very tense. On opening the dura, there was a sudden gush of cloudy spinal fluid, the girl's respiration became better as the pressure was released, but then, the breathing became stertorous and the child died. The father threw himself across his daughter's body and wept uncontrollably.

From our present knowledge, this method of treatment was not only useless but definitely contraindicated. Now we have antibiotics, which they didn't then in the early twenties, and meningitis in our present days is a rare complication following intracranial surgery.

The second great problem was localization of brain tumors.

As previously stated, the localization of a brain tumor was at best 50 to 60 percent since this depended solely on the interpretation of neurological findings.

One day this was radically changed by a resident in surgery who was attending a radiological conference at John's Hopkins. The skull x-ray of a patient with a head injury was being shown. The ventricles of the brain were accurately outlined by air having spontaneously entered the subarachnoid space thru a fracture of the frontal sinus which apparently had nicked the dura. It struck him that if the fluid in the ventricles of the brain could be withdrawn and replaced by air, this could show ventricular displacement to one side or another, this could show which portion of the ventricle was cut off by a tumor and thus more accurate localization of a tumor would be possible. This was the beginning of pneumoencephalography and ventriculography, and Dr. Walter Dandy, a surgical resident, made the greatest contribution to neurological diagnosis in a century. Accurate localization of brain tumors was now possible in 80 to 85 percent of the patients.

A few years later, Dr. Egas Moniz discovered carotid angiography, so that along with air studies it was possible to localize a brain tumor in approximately 90 percent of all cases. With angiography, the histology of many tumors can be determined preoperatively by the peculiar vascularization of the lesion. At present, with electroencephalography and the brain scan, this accuracy in localization has gone to 95 percent. More recently you may have heard of the development of the EMI and ACTA scanner, a computarized axial x-ray scanner which eliminates the necessity for pneumoencephalography and angiography and prints accurate

tumor localization in almost 98 percent of the cases. It is based on computerizing differentials in tissue density and can print pictures of ventricles, clots, vascular malformations, and tumors and can differentiate between neoplasms and infarcts.

The third problem was the control of hemorrhage. It is almost impossible to tie off blood vessels in the brain, except the large vessels, as is done in general surgery. Bleeding was controlled hy pressure and by placing muscle stamps on bleeding points and by the use of silver clips on larger vessels. In the late twenties, Dr. Harvey Cushing introduced the electrocautery, which chars bleeding points. Later followed the development of the present hemostatics like gelfoam and surgicel.

The fourth great problem was the control of brain edema.

It was easy to enter the skull one way or another, but the swollen brain caused by tumor growth and pressure presented a great problem. When the dura was opened under great pressure, the sudden release of this pressure caused such a great surge of brain pushed by the underlying tumor and vascular congestion, that many patients died on the table due to massive brain rupture.

The intracranial pressure was reduced to some extent by doing a spinal tap or ventricular puncture while the patient was on the operating table and the skull was open. But it frequently was not enough, since the brain bulk was so large that too little fluid was often obtained to make much difference. A trick to prevent brain rupture in those times was to turn a very large bone flap and to incise the dura very widely, while at the same time keeping it pressed down over the brain with mosquito clamps attached to the cut edge. When the dural incision was wide enough, the dural flap was suddenly reflected and the brain would bulge into the skull opening, the pressure thus being dissipated over a large area, thus preventing cortical rupture. But now we have urea and mannitol which we give when starting the scalp flap and by the time the bone flap is turned, the brain bulk is reduced by at least 1/5, thus making surgery much safer. Dexamethasone in high doses also helps control brain edema.

Another method of controlling intracranial presusre at operation in certain cases is one that I saw in India. In 1967 I was sent by the Congress of Neurological Surgeons to that country to visit the various neurosurgical centers there. Since there were only 50 neurosurgeons in all of India for a population of 550 million people, you can just imagine what their work load was like.

In the Christian Medical College at Vellore in South India, there were at least 10 patients with posterior fossa tumors waiting for surgery. I was amazed at their good general condition. I was told many of these patients had come in a semi-stupor, but because of the heavy work-load, they immediately had ventricular–atrial shunts placed. This reduced the intracranial pressure and also the pressure against the medulla. The blood supply was thus normalized, and at operation at a more convenient later date, the surgeon worked in a posterior fossa without abnormal intracranial pressure and with more normal anatomical relations. When I returned to Puerto Rico, we adopted this method, and our own mortality rate in posterior fossa surgery dropped from about 15 percent to practically zero.

I am not going to burden you with a recitation of the various tumor types, but will mention just a few things about the more common brain tumors generally.

There are benign tumors and malignant tumors as anywhere else in the body. One characteristic of malignant brain tumors is they practically never metastasize. A tumor like a meningioma is benign and when completely removed is curable; but, if this tumor envelopes the internal carotid artery and the optic nerve, as in many cases of medial sphenoid ridge meningiomas, it can only be partially removed and will recur. This tumor then may be said to be malignant because of its position. Low grade astrocytomas, when they occur in the frontal or occipital lobe tips or the non-dominant temporal lobes, can be completely excised by removing the entire lobe with the tumor inside. Cystic astrocytomas are curable if the nubbin of tumor deep in the cyst is excised.

Pituitary tumors when affecting the optic nerves are evacuated either thru a frontal craniotomy, and the patient then sent for cobalt therapy. Or, the tumor nodule can be discreetly dissected out by means of the transnasal approach with the use of an operating microscope. After complete removal of the adenoma, the rest of the pituitary gland is left intact. Those pituitary tumors that have not yet encroached on the optic nerves are notoperated but sent for radiotherapy. This is also done with brainstem tumors. Suprasellar cysts are evacuated or removed completely when possible.

The most distressing tumor is the astrocytoma grade III and IV or the so-called glioblastoma multiforme. This tumor constitutes 40 percent of all the brain tumors of adults. By the time the symptoms

become manifest, the tumor has frequently sent cells across the corpus callosum or to other contiguous areas of the brain out of the surgeon's reach. The usual life span from onset of symptoms to death, with or without surgery, is less than a year.

The neurosurgeon is thus faced with the decision whether it is advisable to merely take a biopsy for diagnosis, and if positive for glioblastoma to close the wound and give the patient radiotherapy, or to turn a flap and remove as much tumor as possible and then send the patient for radiotherapy and chemotherapy, for it is practically certain that although the patient will get some relief from the decompression and subsequent treatment, the tumor will grow, the patient again will begin with headaches, weakness and disturbed consciousness and again go through all the agonies incident to terminal brain tumor.

Yet there are reports of glioblastoma patients living much longer. We operated on one of our patients three times for a frontal lobe glioblastoma, which extended his useful life for more than 7 years.

Tumors in the dominant hemisphere, like the left temporal lobe in right-handed people, are actually inoperable from a functional standpoint, because surgery in that area will leave the patient with a sensory aphasia and make it impossible for him to communicate with others.

To my regret I operated on one such patient under peculiar circumstances. He was a 48 year old army sargeant at Fort Brooke who had a common-law wife and seven children. The priest came to implore me that I operate on this man to allow him to regain consciousness so that he could marry his common-law wife and legitimize his children. I operated and the ceremony took place several weeks later, but the patient lived for months in a state of agonizing frustration and tears being unable to express his thoughts or interpret what was being said to him. He was a human being completely alone in a world crowded with people.

There is a practice in some centers to keep a patient on high doses of dexamethasone without any other type of treatment once a glioblastoma or metastatic tumor is diagnosed by noting its vascular supply on angiography. It seems that not much time for life is gained with any type of treatment now used for glioblastomas except in rare instances.

Perhaps one of the major problems in neurosurgery, even to this day, is that physicians generally do not think of the possibility of brain tumor, so that, when the classical symptoms of headache, visual disturbances, paralysis and vomiting appear, the lesion is pretty far advanced. The case is then not only more difficult to handle, but the patient has already suffered irreparable neurological damage. This is true for benign as well as for malignant tumors.

The key to successful neurosurgery is the early referral of these patients. Brain tumors are not uncommon; they comprise between 5 to 7 percent of all body tumors.

Tumors of the central nervous system can simulate other conditions. Thus a thoracic tumor if high may simulate gall bladder pain while one lower down, kidney stone radiation. Some parasagittal tumors can compress the brain areas on either side of the falx that control the voluntary initiation of micturition, resulting in urinary retention simulating prostatic obstruction. G. I. upsets, especially in children, may be the first sign of posterior fossa tumor.

Let me present two cases:

After giving birth to her fourth child, this 32 year old woman became concerned when her menses had not returned after six months. She went to her gynecologist who told her not to worry, that in some women there is such a delay. When after a year she still had no menses, the patient was told that she had an early menopause. After visiting three more gynecologists in the next year and being told the same thing, the patient reluctantly gave up seeking help. She then developed headaches, and a psychiatrist told her that she was suffering from a sort of self-degradation based on her fear of decreased womanhood. Her libido decreased, and she began to experience some visual difficulties.

She returned to several other physicians and ophthalmologists who corroborated the opinions of the previous doctors. Now after four years the patient went to see still another doctor, and she repeated the same story that she had been doing for the past years: "Doctor, she said, I have lost my menses, I have decreased sexual desire, I have headaches and I can't see as well as I did before...."

The story is so clear. The last doctor sent her to an ophthalmologist who found bitemporal cuts on visual fields, some optic atrophy and a large sella turcica on x-ray.

How is it possible for a patient to recite typical symptoms to ten physicians over three or four years and not one pick up its meaning? The patient was operated for a cystic pituitary tumor, and when I last saw her two months ago — three years after surgery, she was doing very well, having recovered some of her lost vision.

The second story is that of the niece of one of the officials of the government of the little island of Anguilla. This 11 year old child began to experience nausea on arising in the morning. As the weeks passed, she began to vomit and had occasional mild headache. She was sent to one of the larger British Islands where her appendix was removed. The symptoms persisted and after extensive G. I. studies in Saint Thomas, she was sent to the Presbyterian Hospital in San Juan.

Funduscopic examination showed a 3+ papilledema with hemorrhage and exudates. The child was dehydrated and weak with a hemoglobin of 8 grams, hardle able to walk. Ventriculography showed large lateral ventricles. An A-V shunt was done and in the next few days the patient was out of bed. During the next two weeks, the general physical health of the patient improved and the girl became practically normal. At operation a benign arachnoidal cyst was removed from the posterior fossa; and, when I inquired about the patient several weeks ago, I was told she was married and had just delivered her first child.

Now, what is the obligation of a physician to his patient? It is not to know every specialty thoroughly. But it is to be familiar in a general way with the different medical fields so that referral to the proper specialty is possible.

Yet of all the patients seen by doctors, patients with neurological conditions are the least likely to have such early referrals. One does not have to know much neurology to detect early neurological abnormalities.

The classical symptoms of intracranial tumor which we are taught in medical school, which are headache, visual disturbances and vomiting, should perhaps be forgotten. These are symptoms that appear rather late with increased intracranial pressure. There are other early signs that can lead one to suspect the presence of an intracranial tumor.

The one most certain picture of a growing intracranial mass is a non-febrile slowly progressive change in neurological function, decrease in visual acuity which is poorly corrected by change of glasses, decrease in hearing on one side, some awkwardness in the handling of usual chores, progressive weakness in one or more extremities, mild unsteadiness of gait, change in personal habits, unexplained change of character, difficulty in identifying familiar objects, and convulsions.

All of these are changes for which no special neurological knowledge is necessary, but they should alert one to the early changes in neurological function. It is not too much to ask the physician to be on the look-out for just such minor variations.

Thus by overcoming four major obstacles, (1) accurate brain-tumor localization before operations, (2) control of infection, (3) control of hemorrhage, (4) control of brain swelling, brain surgery in the span of 60 years has passed from a prohibitively dangerous field of surgery with a tremendously high mortality to a highly skilled, accurate, relatively safe specialty with a mortality percentage not higher than most major surgery. Now, the outlook for cure in patients with brain tumors, which are benign, is exceedingly good, and for those with brain tumors that are malignant, prolongation of life is increasingly promising.

IS MONOCULAR TESTING IN PRESBYOPES USEFUL?

Manuel N. Miranda, MD

After determining the distance correction of a presbyopic patient for each eye separately, most ophthalmologists prescribe equal bifocal additions without first trying these out monocularly. With additions thus prescribed most patients will be comfortable; because the accommodation reserve is usually equal in both eyes (1). However, a small percentage of patients will return to the ophthalmologist with the complaint of seeing the reading material better with one eye than with the other; or of seeing clearly with either eye, but at different distances; or of seeing better with either eye than with both together. Such complaints can be avoided, if monocular tests are made before determining the bifocal additions.

Case Presentations and Discussion

Case 1:

A woman, 48, had been given the following prescription:

O.D. +2.00 sphere
O.S. +2.50 sphere
add +1.75 O. U.

She complained of reading less clearer with the right eye.

Examination had revealed 20/100 in each eye, without correction, an amplitude of accommodation of 2D in both eyes, and a reading distance of 13 inches. Her vision improved to Jaeger 1 in each eye with the prescription at near, but she was able to see better with the left than with the right eye. After increasing the correction of the right eye to +2.25, she was able to see equally clearly with either eye at distance as well as at near.

Her right eye had been slightly undercorrected. Had the bifocal additions been determined monocularly, this undercorrection would probably have been uncovered. When monocular tests reveal the need of unequal additions, the most frequent cause is a spherical imbalance in the distance correction, usually an "under plus" of one eye (1, 2).

Case 2:

A male, 25, was wearing the following prescription:

O.D. +4.00 sphere
O.S. −1.50 sphere +0.50 x 90°

which gave him 20/20 vision in each eye. He complained of a difficulty at his working distance of 13" where he saw well with his left, but not with his right eye. His amplitude of accommodation was 8 D in each eye.

In anisometropia such as this the accommodative requirements for the two eyes are different for the same object distance (3). The following formula (4), supplied to me by Dr. Paul Boeder, gives the approximate accommodative requirement, A', for corrected ametropic eye in terms of An, the accommodative requirement for an emmetropic eye at the same working distance, when the distance correction, Dc, is mounted 12 mm, in front of the cornea:

$$A' = An + (3\ Dc) \text{ percent of } An$$

According to this formula the right eye of the patient had to accommodate

$$A' = 3.00 + 12 \text{ percent of } 3.00 = 3.36 \text{ D}$$

whereas the left eye had to accommodate

$$A' = 3.00 - (3 \times 1.50) \text{ percent of } 3.00 = 2.86 \text{ D}$$

with a bifocal addition of +.50 D in the right eye the patient had clear monocular and binocular vision at the working distance.

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Presentado en la Reunión Anual de la Sección de Oftalmología de la Asociación Médica de Puerto Rico en el Hotel Cerromar de Dorado, Puerto Rico, en julio de 1975.
Favor de solicitar reproducciones a: Manuel N. Miranda, GPO Box D, San Juan, Puerto Rico 00936.

Case 3:

A dentist, 40, was given the following prescription:

OD $-3.50 -0.50 \times 90^{o}$
OS $+1.50$ sphere
add $+0.75$ O.U.

He worked at a distance of 13 inches and saw clearly with the right, but not with the left eye. However, when moving his head back he saw clearer with his left eye. His amplitude of accommodation was 4 D in each eye.

Since he worked for long hours at 13 inches it was advisable not to let him use more than 2.00 D of accommodation, that is, half his amplitude. In this case, therefore, A' is known, and we have to solve the equation for An (4) in terms of A'. Thus,

$$An = A' - (3\ Dc) \text{ percent of } A'.$$

Substituting the known values for the right eye, we have

$$An = 2 - (3 \times -3.50) \text{ percent of } 2 = 2.21 \text{ D}$$

This is what the right eye is getting out of an accommodation of 2D through the sphere of -3.50 D. It falls .79 D short of $+3.00$ D which is required for the working distance of 13 inches. Therefore, a bifocal of $+0.75$ D was added to the right eye lens.

For the left eye we obtain

$$An = 2 - (3 \times 1.5) \text{ percent of } 2 = 1.91 \text{ D}$$

This falls short of 3.00 D by 1.09 D. Therefore, a bifocal of $+1.00$ D was added to the left lens. With this change of the bifocal addition in the left eye the patient had very satisfactory vision.

About 10 percent of all presbyopes require a different addition for each eye. Not all due to an spherical imbalance in the distance correction or to an anisometropic unequal accommodative requirement as many actually have differences in the amplitude of accommodation of both eyes. Some may even show more than one reason for an unequal addition. The following case presentation exemplifies that:

Case 4:

A female, 50, needed the following prescription:

O.D. $-5.00 -0.75 \times 175$
O.S. Plano
add $+1.00$ O. D. at 13"
add $+2.00$ O. S. at 13"

With that prescription she had 20/20 vision in each eye and Jaeger 1 each eye for reading at 13".

The accommodative requirements for the two eyes, according to the formula A' = An $+(3$ Dc) percent of An, were:

Right Eye A' = $3.00 - (3 \times 5)$ percent of $3.00 = 2.55$ D
Left Eye A' = $3.00 + (3 \times 0)$ percent of $3.00 = 3.00$ D

The accommodative requirement was 2.55 in the right eye. She accepted an addition of only $+1.00$ D as she was contributing 1.5 D from her amplitude of accommodation that was 3.00 D in that eye.

The accommodative requirement was 3.00 D for the left eye. She accepted an addition of $+2.00$ D as she was contributing only 1.00 D from her amplitude of accommodation that was only 2.00 D in that eye.

This case shows the need of unequal bifocal additions for the two eyes, not only because of an unequal accommodative requirement imposed by anisometropia, but also to a difference in the amplitude of accommodation of both eyes.

Conclusion

Monocular testing in presbyopes is useful. It will serve as a double check for the distance refraction, will make possible the correct unequal bifocal addition required by anisometropes and patients with aniso accommodation, and will cut down the number of dissatisfied patients.

Summary

Monocular tests may uncover imbalances in the distance correction of the two yees, the need for different bifocal additions in anisometropia, and differences in the amplitudes of accommodation of the eyes.

Resumen

Pruebas monoculares pueden descubrir desbalances en la corrección de distancia de los dos ojos, la necesidad de adiciones desiguales en el bifocal en anisometropia y diferencias en la amplitud de acomodación de los dos ojos.

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ACREDITACION DE LA ESCUELA DE MEDICINA EN EL AREA DE EDUCACION MEDICA CONTINUADA

Egidio S. Colón Rivera, MD

Existen al presente tres áreas definidas en el campo de la educación médica que son: enseñanza a los estudiantes de medicina (undergraduate medical education), el programa de residencias (graduate medical education), y la educación médica continuada (continuing medical education). Cada una de estas tres áreas tiene su programa de acreditación y, hasta el presente, nuestra Escuela de Medicina está acreditada para la enseñanza de estudiantes de medicina, como también está acreditado el programa de residencias. La única área que estaba pendiente de acreditación era el área de educación médica continuada. Debido a muchos factores, entre ellos principalmente a la inseguridad de que este programa no se pudiera continuar, no se había solicitado formalmente el que se nos visitase para fines de acreditación.

Por varios años hemos estado en contacto con el Dr. Rutledge W. Howard, Director Asociado del Departamento de Educación Médica Continuada de la Asociación Médica Americana en relación a dicha acreditación, pero no fue hasta fines del año 1974 cuando se decidió a proceder a iniciar los trámites de dicha solicitud. La Asociación Médica Americana nombró un grupo (Survey Team) para que nos visitase, presidido por el Dr. Ralph C. Sánchez, Decano Asociado de Educación Médica Continuada de la Universidad Estatal de Louisiana, junto con el Dr. Germán Lasala, Presidente del Consejo de Educación Médica de la Asociación Médica de Puerto Rico y la Dra. Magda Pendall de Islas Vírgenes. Dicha visita tuvo lugar el lunes 18 de agosto de 1975. Ellos revisaron los objetivos del programa, las normas administrativas, el presupuesto, la facultad, el curriculum, las facilidades, los métodos educativos y los métodos de evaluación. Como parte de la visita, se entrevistaron con el Decano de la Escuela de Medicina, algunos Jefes de Departamento, algunos miembros de la facultad participante, con miembros del Comité de Educación Médica Continuada, con estudiantes del CURSO y con el personal de la oficina. También visitaron el salón de clases para observar la enseñanza e inspeccionar las facilidades existentes. Al final se reunieron en sesión ejecutiva y se nos notificó que dicho programa había sido aceptado, pero que dicha recomendación tendría que pasar por los canales usuales en la Asociación Médica Americana antes de que nosotros recibiésemos la notificación oficial de dicha decisión; pero, que cuando se recibiese, sería efectiva desde el día *18 de agosto de 1975.* Esto quiere decir que desde el 18 de agosto de 1975 cualquier programa de Educación Médica Continuada que esté aprobado por la División de Educación Médica Continuada tendrá crédito para la Categoría 1 del "A.M.A. Physicians Recognition Award."

Dicha aprobación esperamos que tenga un gran impacto en la educación médica continuada en Puerto Rico ya que facilitará el coordinar los esfuerzos en dicha área y hará posible tener un programa más abarcador que la actividad principal de la División que ha sido hata el presente el CURSO DE ACTUALIZACION MEDICA. Con este paso de avance la Escuela de Medicina podrá ser efectivamente la que asuma el liderato en dicha área y podrá llevar a cabo un programa que desarrolle los siguientes aspectos:

1. **Acreditación de cursos de Educación Médica Continuada:**

   Todas las instituciones que estén asociadas formalmente con la Escuela de Medicina tendrán derecho a que sus actividades en el campo de la educación médica continuada puedan ser aprobadas por la División. Aquellas actividades que se programen para fechas específicas, con suficiente anterioridad, podrán aparecer en la lista anual de cursos que publica la A.M.A. en el número de a mediados de agosto del "Journal of A.M.A." Una lista parcial de dichas

Consultor en Educación Médica Continuada, División de Educación Médica Continuada, de la Escuela de Medicina de P. R.

instituciones y grupos podría incluir todas las instituciones que componen el Centro Médico, los Consorcios, el Programa Médico Regional y otras. Esto facilita grandemente el proceso de acreditación, pues en vez de tramitar dicha acreditación directamente con la Asociación Médica Americana o con la Asociación Médica de Puerto Rico que implica un proceso largo y laborioso o que en algunos casos no es permitido, lo único que tendrían que hacer es preparar:

1. Objetivos de dicha actividad.
2. Descripción de la actividad.
3. Lista de participantes con sus direcciones.
4. Método de cotejar asistencia.
5. Certificado de asistencia.
6. Programación hora por hora de tópicos y actividades.
7. Lista de los diferentes métodos de enseñanza que sean utilizados Ej. casettes, video tapes, películas, etc.

Dicha información se discutiría previamente con la División y no se visualiza ninguna dificultad en que dichas actividades sean aprobadas; por el contrario la División lo que quiere es fomentar el que hayan más y mejores actividades en esta área de educación médica continuada.

2. Certificado de Reconocimiento al Médico (Physicians Recognition Award):

Dicho certificado es utilizado para reconocer la labor del médico que participe regularmente en programas de educación médica continuada cuyo propósito es mantener y mejorar su competencia como médico y cuya finalidad es mejorar el cuidado del paciente. Dicho certificado lo concede la Asociación Médica Americana a aquellos médicos que se hacen acreedores al mismo. Se concede por un período de tres años y durante esos tres años debe haber cualificado para un mínimo de 150 horas de crédito en diferentes categorías (seis). Las actividades docentes auspiciadas por la División cualificarían para la categoría 1, que son las auspiciadas por instituciones acreditadas. Este certificado se está aceptando por las Asociaciones Médicas Estatales que exigen evidencia de educación médica continuada como requisito para ser miembro de las mismas y también por la Junta Examinadora de Médicos de Maryland y Nuevo Méjico para cumplir con el requisito de educación médica continuada a los que deseen renovar su licencia para practicar medicina.

Consideramos que la División debe estimular el que todo médico que cualifique tenga su Certificado, ya que esto comprueba que el médico se está manteniendo al día. Además, el que la Escuela de Medicina haya sido acreditada, facilita el que más médicos puedan cualificar para dicho Certificado. La oficina de la División estaría disponible para ayudar a llenar dichos blancos y contestar preguntas en relación a los mismos.

3. Organización para Revisar las Normas Profesionales (P. S. R. O.):

La educación médica continuada es un componente esencial del P. S. R. O. En dicho programa se podrán identificar los problemas que afecten el cuidado médico del paciente que se deban a deficiencias en conocimientos médicos y para los cuales se requeriría una solución basada en la enseñanza de dichos conocimientos. La División podría auspiciar programas debidamente acreditados y diseñados para corregir dichas deficiencias.

En resumen, el que la Escuela de Medicina haya sido acreditada en el Area de Educación Médica Continuada, debe resultar en un programa más vasto y abarcador en dicha área. Esto eventualmente, redundará en una mejor atención médica del paciente que es nuestra meta final.

FROM THE WASHINGTON OFFICE OF AMERICAN MEDICAL ASSOCIATION

The public interest would be better served if the nation examined the goals of a national health insurance program within the context of the existing health care system and directed its energies toward the perfection of that system, the American Medical Association said in testimony before a subcommittee of the House Interstate and Foreign Commerce Committee.

"It is unnecessary to gamble on a whole new medical health system in order to meet the health care needs of all Americans," AMA president Max H. Parrott told the Public Health and Environment Subcommittee.

Pointing to the large problems involved in creating a national health insurance program, Dr. Parrott, a Portland, Ore., practitioner, said that public attitudes toward it are changing steadily.

"These problems have been brought into better focus as a result of evidence of the effects of governmentally administered and controlled programs both here and abroad.

"Our national priorities have also shifted because of the effects of the changing economy, and the devastating effects of inflation on all segments of our society.

"Significant changes have taken place in our health system through increased manpower programs, increased facilities construction, increased levels of private health insurance coverage, and a variety of other programs. There is fuller realization and acknowledgment that this country's health system—under attack by many in the course of the NHI debate—is indeed superior to any other in the world," Dr. Parrott said.

Dr. Parrott told the subcommittee members of the medical profession's national health insurance plan (H. R. 6222) which builds on the structure of the present system of employer-employee group health insurance plans, mandating each employer to provide comprehensive and catastrophic benefit coverage with the employer picking up at least 65 percent of the cost.

Employees, according to the AMA spokesmen, would not be compelled to participate. The self-employed as well as the non-employed could purchase qualified private health insurance, through pools if needed, at a cost not more than 125 percent of the cost of group plans. And, after a certain level of co-insurance is reached, depending upon income, the insurance would cover all remaining costs as a complete protection against catastrophic costs.

Dr. Parrott pointed out that in pressing for the adoption of any particular NHI proposal, sincerity must not be confused with objectivity—"We cannot afford to have a program of such importance fail.

"We must avoid the mistake inherent in those proposals which would lock medicine into a rigid, monolithic, no-choice bureaucratic system. Such a creation would be impossible to reverse. It would be an undertaking full of promise but empty of fulfillment. Establishment of cost control through fixed budgets including arbitrary fee schedules would result in curtailment of care and discourage participation by providers.

"A look at the current trouble of the British health care system impels a close re-examination of the alleged need for such drastic action," Dr. Parrott said.

****

The Senate Finance Committee also approved with few changes Medicare Amendments adopted earlier by the House. The major one assures that no prevailing Medicare fee for this fiscal year is less than for the previous fiscal year. An unintended effect of the new law tying physicians Medicare reimbursement in with a cost-of-living-type index was to roll back some fees. HEW didn't want to do anything about it, but the House at the urging of the AMA and other groups, agreed to prevent the rollback.

The Senate Committee added language to the House provision to indicate that in calculating the controversial fee index HEW should include to the extent feasible "factors related to any increases in costs of malpractice insurance and that index calculations should be prepared on a regional rather than a national basis."

The other Medicare changes include:

—A one-year extension of authority to grant waivers of nursing staff requirements in rural areas where nurses are in short supply. The House had approved a three-year extension.

—Repeal of a present provision which would make the Federal Employees Health Program rather than Medicare the primary payer of benefits for older or retired U. S. workers. The amendment specifies that Medicare be the primary payer for people eligible for both programs.

HEW NEWS:

The Department of Health, Education, and Welfare published final regulations which limit the liability of physicians, and other providers of services, and Medicare beneficiaries for incorrect Medicare payments, particularly those discovered more than 3 years after the year in which they



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were made.

The regulations, which become effective with their publication in today's issue of the *Federal Register,* implement provisions of the 1972 Social Security Amendments.

The new regulations provide that a Medicare provider, physician, or supplier of Medicare items who was incorrectly paid through no fault of his own will not be required to refund the incorrect payment.

Also, an incorrectly paid provider, physician, or supplier will be deemed to have been without fault, in the absence of evidence to the contrary, if the payment was determined to be incorrect later than the third year after the year in which it was made.

In these situations, the Department said, responsibility for the incorrect payment shifts from the provider, physician or supplier to the beneficiary. However, the Social Security Administration will waive recovery of incorrect payments from beneficiaries who were without fault, if recovery would cause the beneficiary economic hardship, would deprive him of necessary medical care or would be unfair for some other reason.

The new regulations also contain two provisions which limit the liability of beneficiaries where an incorrect payment has been made. If a payment is determined to be incorrect later than the third year after the year in which it was made, there will be no recovery from the beneficiary if he was without fault; i.e., waiver will be automatic. Also a provider, physician, or supplier who is responsible for refunding such an incorrect payment may not send a bill for the amount involved to a beneficiary who was without fault. These two provisions recognize that a Medicare beneficiary ordinarily is not in a position to know whether medical services furnished him are covered under the program, the Department said.

The new regulations were slightly revised to take into account comments received from the public as a result of their publication as proposed regulations in the April 18, 1974 Federal Register.

THIRD ANNUAL ASPEN MUSHROOM CONFERENCE - HOTEL JEROME - ASPEN, COLORADO - AUGUST 8-13, 1976.

For further information contact: Aspen Mushroom Conference, 1818 Gaylord Street, Denver, Colorado, 80206. (303) 320-5333.

FROM THE AMERICAN MEDICAL ASSOCIATION:

A BILL PROPOSING REGULATION OF THE OPERATION and use of radiologic equipment "would give an unprecedented authority to the federal government to regulate and to control educational program and personnel related to essential health care services," the AMA said in a letter to the House Public Health and Environment Subcommittee. The bill (HR-559) would impose federal standards and criteria for accreditation of schools teaching radiologic technology and for the licensure of radiologic technologists. It would also establish criteria "for education institutions conducting programs for the training of medical and dental practitioners. The AMA said, "This proposal is unnecessary and unwarranted, and we recommend its rejection."

The Bill Would Duplicate certification and accreditation activity now effectively implemented through professional organizations and would abrogate the constitutional power of states to regulate health professions and occupations, the AMA said. There is no compelling evidence that universal licensure of radiologic technologists, even at the state level, is in the public interest, the statement points out. "The standards established by professional groups for such regulation or certification.... are all set at a higher level than are those for licensure."

In Requiring the HEW Secretary to issue criteria for medical and dental educational institutions, the bill "is startling in its implications," the AMA said, adding: "It makes an assumption of government competence to determine content of education programs. Our medical and dental schools are highly respected throughout the world, and their programs.... should not be dictated by government. Government should not impose curriculum content or instructional procedures upon professional staff in medical and dental education and training programs."

ENACTMENT OF PROPOSED HMO AMENDMENTS would amount to a decision by Congress that the health maintenance organization concept is invalid and has been abandoned, the AMA told the Senate Subcommittee on Health. In testimony scheduled to be given Jan. 19, Edgar T. Beddingfield Jr., MD, vice chairman of the AMA Council on Legislation, said the purpose of the HMO act was to create demonstration projects to ascertain whether the HMO concept, as passed by the House, would reduce required basic services; make supplemental services optional; defer community rating of premiums; delete the requirement for open enrollment, which would permit "skimming" and elimination of unfavorable risks; and would remove the requirement that a medical group be primarily engaged to provide the services.

The Amendments Would Eliminate those characteristics which distinguish the "HMO" from other prepaid group practices, Dr. Beddingfield said. The proposed amendments would "convert a demonstration health delivery program into a mechanism for the funding of ordinary prepaid groups," he pointed out. "Because this result would be so far beyond the initial intent of the original act, fairness requires that the act would have to be amended to delete the phrase "health maintenance organization."

The AMA Urged That The Present Experiment be continued without change. "In our opinion," Dr. Beddingfield said, "the public deserves an answer as to whether the HMO, conceived after extended debate and promising accessible comprehensive care in a manner superior to other modes of health care delivery, is a viable concept."

THE START OF HEARINGS ON THE FTC ANTITRUST COMPLAINT against the AMA has been delayed two weeks at the request of AMA attorneys. An answer to the change that the AMA *Principles of Medical Ethics* proscription on advertising by physicians is in restraint of trade will be filed by the AMA on Jan. 23 and the hearings will begin Feb. 25. The hearings will be before a Federal Trade Commission administrative law judge in Washington, D. C. Also named in the FTC complaint are the Connecticut State Medical Society and the New Haven County Medical Assn. (See *AMA Newsletter,* 1-12-76).

Just a Week Before The FTC issued its complaint the Board of Trustees of the American Dental Assn. had resffirmed its policy that advertising by dentists is a breach of professional ethics. The ADA action was in response to a proposal by the Alaska Dept. of Commerce and Economic Development that would make it unlawful for licensing agencies and professional associations to prohibit advertising in the state. An editorial in the *ADA News* took issue with the FTC complaint against the AMA: "The Federal government, through its various agencies, seems determined to gradually break down and completely destroy the traditional characteristics of professionalism in this country.... Past experience strongly suggest that blatant advertisement of health services misleads the public in regard to the quality of service to be received and the fee involved."

THE AMERICAN BOARD OF FAMILY PRACTICE ANNOUNCES THE NEXT CERTIFICATION EXAMINATION WILL BE GIVEN OCTOBER 30-31, 1976. The two day written examination will be held in seven cities geographically distributed throughout the United States. Information regarding the examination may be obtained by writing:

Nicholas J. Pisacano, MD, Executive Director & Secretary
AMERICAN BOARD OF FAMILY PRACTICE, INC.
University of Kentucky Medical Cente r
Lexington, Kentucky 40506

Please note: It is necessary for each physician desiring to take the examination to file a completed application with the Board office. DEADLINE FOR RECEIPT OF APPLICATIONS IN THIS OFFICE IS JUNE 15, 1976.

ARTICULOS A PUBLICARSE EN LA EDICION DE ABRIL 1976

1. Leptospirosis in a Rural Barrio of Guaynabo, Puerto Rico - *Robert A. Hiatt, M. D. and Catherine R. Sulzer, B.S.*

2. Vitamin B_6 Intake and Urinary Excretion of 4 Pyrodoxic Acid per gram of Creatine in a Rural Puerto Rican Area - *Nelson A. Fernández, M. S. M.IC.*

3. Recent Advances in External Pulse Recordings - *Juan M. Aranda, M. D. and Benjamín Befeler, M. D.*

4. Protesis de Pene "Small-Carrión". Nuevo Suplante para el Tratamiento de la Impotencia - *Michael P. Small, M. D. y Hernán M. Carrión, M. D.*

5. Foro de Medicina Nuclear - Pulmonary Embolism - *Freida Silva de Roldán, M. D. y Raquel Martínez, M. D.*

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Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.
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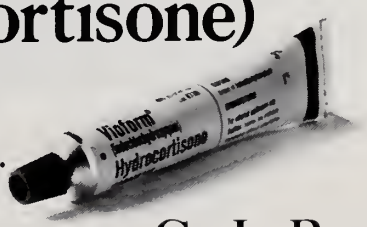
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item:	**Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.**
item:	**Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, *fewer than 1 in 5* women practice BSE, and *only half* have an annual breast examination by a physician.**
item:	**Only 35% of all women polled reported that a *physician* had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.**
item:	***But*, among women who received personal instruction from their physicians, the overwhelming majority *(92%)* practiced BSE during the preceding year.**

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE.

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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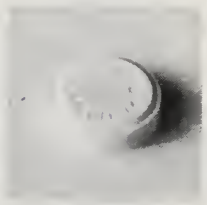
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in psychoneurotic anxiety states with associated depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

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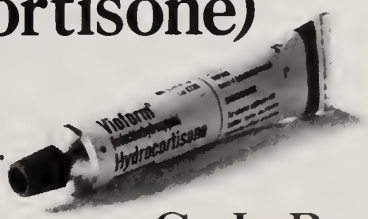
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Volumen 68 Abril 1976 Número 4

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PORTADA: EDIFICIO ATENEO PUERTORRIQUEÑO

LEPTOSPIROSIS IN A RURAL BARRIO OF GUAYNABO, PUERTO RICO

Robert A. Hiatt, MD
Catherine R. Sulzer, BS

Leptospirosis is an infrequently reported zoonotic disease with a wide range of clinical manifestations. It is often incorrectly considered a rare disease and therefore is included in the differential diagnosis only in cases of severe febrile illnesses associated with jaundice. In recent decades the worldwide distribution and varied epidemiologic and clinical nature of this disease have been more clearly defined, although much about its mode of transmission, true incidence, and pathogenesis remains an enigma. Our current knowledge of human leptospirosis has been reviewed extensively by several authors (1-4).

In Puerto Rico leptospirosis was probably first identified as "spirochetes" in the urine of a jaundiced patient in 1918 (5), but its presence was not documented until 1939 (6). Studies of the disease in Puerto Rico in the early 1950's resulted in the detection and reporting of a large number of cases and a number of publications on clinical and laboratory aspects of the disease (7-13). The epidemiologic aspects of these studies were described in an extensive monograph by Alexander *et al* (14). Since that time, however, no new or up-to-date information is available. Only 7 cases were reported to the Center for Disease Control (CDC) from Puerto Rico in the decade between 1964 and 1975 (15), and most of these diagnoses were based on serologic evidence alone. This is in striking contrast to the 208 confirmed cases that Alexander *et al* reported in the 4-year period between 1948 and 1952 (14). It is unlikely that the incidence of leptospirosis has dropped so dramatically in Puerto Rico, especially in light of the fact that there has been an increase in cases reported to the CDC in the United States in recent years (15). It is more likely that leptospirosis in Puerto Rico has not been diagnosed as frequently because of a low index of suspicion on the part of physicians, a lack of diagnostic resources, and incomplete reporting.

The present study reports on a survey of leptospirosis in a rural barrio of Guaynabo, Puerto Rico. Data on human seroreactivity as well as culture and serologic studies in domestic animals and wild rats in the neighborhood revealed evidence that the organism is well established in several hosts and reservoirs. Ecologic and epidemiologic aspects of the infection are described in hopes of stimulating more awareness of leptospirosis and greater interest in its study and control in Puerto Rico.

Methods

In August 1974, a case of acute febrile illness in a 10-year-old girl drew attention to leptospirosis as a possible diagnosis. The illness was characterized by meningeal irritation, nonpurulent conjunctivitis, a generalized macular rash, malaise, confusion, and shock; she died on the sixth day of her illness. Before her death, historical information indicated that she had been swimming in a stream located in a cattle pasture on a farm near her home in Barrio Santa Rosa I, Guaynabo. An epidemiologic investigation was begun to see if there was supportive evidence for the diagnosis of leptospirosis and, if so, to identify the source of infection. Leptospirosis was never documented in the girl despite intensive laboratory investigation and an autopsy.

Human Related

Forty-three residents of the immediate neighborhood where the girl had lived cooperated with the investigation by providing paired serum specimens taken at an interval of 3 weeks. These individuals volunteered after a general request was made for serum specimens from neighbors of the girl and from persons who had been in the stream where the girl had swum. Standardized histories were obtained which included questions on symptoms and illness compatible with leptospirosis during the last year as well as on animal and water exposure.

Sera were frozen and packed in ice and sent to the Leptospirosis Reference Laboratory, CDC, Atlanta, Georgia. The specimens were first screened with 22 serotypes by the microscopic-agglutination test (MA), and those sera found positive were titered to end point with the MA (16). A titer of 1:100 is considered significant evidence of contact with the

From the San Juan Laboratories, Bureau of Laboratories, Center for Disease Control, Public Health Service, U. S. Department of Health Education and Welfare, GPO Box 4532, San Juan, Puerto Rico 00936 and the FAO/WHO Collaborating Center for the Epidemiology of Leptospirosis, Bacterial Immunology Branch, Center for Disease Control, Atlanta, Georgia 30333.

TABLE I
POSITIVE LEPTOSPIRAL SEROLOGIC RESULTS OF PAIRED SERA FROM 43 INDIVIDUALS, BARRIO SANTA ROSA, GUAYNABO, PUERTO RICO, AUGUST-SEPTEMBER 1974

		SERUM 1		SERUM 2	
Age	Sex	Titer	Serotype	Titer	Serotype
8	F	1:50	*copenhageni*	*NR	
10	M	NR		1:100	*butembo*
11	F	NR		1:50 1:200	*butembo* *andamana*
13	M	1:50	*autumnalis*	NR	
14	F	NR		1:100	*autumnalis*
17	M	1:50	*ballum*	NR	
32	F	1:200	*copenhageni*	1:1600	*copenhageni*
32	F	1:100 1:50 1:50	*copenhageni* *autumnalis* *mankarso*	1:400 1:200	*copenhageni* *autumnalis*
37	F	1:400 1:50	*autumnalis* *alexi*	1:200 1:200 1:400	*autumnalis* *icterohaemorrhagiae* *mankarso*
46	F	1:1600 1:200 1:400	*copenhageni* *bataviae* *mankarso*	1:3200 1:800 1:100	*copenhageni* *bataviae* *autumnalis*
49	M	1:100 1:100	*copenhageni* *bataviae*	NR	
50	F	1:50	*bataviae*	1:400	*bataviae*
50	M	1:100	*bataviae*	NR	
62	F	1:200	*bataviae*	NR	
64	M	1:400 1:50 1:50	*copenhageni* *bataviae* *mankarso*	NR	

** - NR - nonreactive*

organism, and a titer change of fourfold or more is diagnostic of recent infection.

Animal Related

On the farm where the pond suspected of being the source of infection was located, five domestic cattle that grazed in the surrounding pasture and one dog were bled by venipuncture. Blood was also drawn from one dog living in the neighborhood of the deceased girl and having a recent history of a severe icteric illness. Urine was obtained from 4 of the 5 cattle at the time of venipuncture. Both blood and urine were inoculated immediately into Ellinghausen polysorbate semi-solid medium (16, 17). Urine from the cattle was also preserved in 0.25 percent formalin (1 ml for each 5 ml of urine) and examined by the direct fluorescent antibody (FA) technique for detection of leptospire oganisms.

Fourteen rats (*Rattus* species) were captured over a period of 2 months from the deceased girl's neighborhood and the area of the farm-house where the stream was located. They were first anesthetized, and blood drawn by direct cardiac puncture and urine obtained transabdominally were inoculated into Ellinghausen semi-solid medium. The rats were then dissected aseptically, and small portions of macerated kidney and brain tissues were also inoculated into the semi-solid medium.

Results

Serologic Survey of Human Population

Serologic results were obtained on 43 paired sera. Table I presents the titers and serotypes of those persons who had a positive reaction. The sera from 8 (19 percent) had a fourfold titer change, indicating recent infection. Titers increased in four persons and decreased in four. The geometric mean titer (GMT) for the first serum samples taken from this group of eight was 1:122.3, with a range from zero to 1:1600. For the second samples taken 3 weeks later, the GMT was 1:125.7 with a range from zero to 1:3200. Most of the diagnostic titer changes occurred in older persons (7 of 13 adults over 15 years of age), and only one of 30 children 15 years or younger was included in the group with fourfold titer changes. The primary serogroups identified were *icterohaemorrhagiae* in three, *bataviae* in three, and one each of *autumnalis* and *andamana*. Five of the eight with significant titer changes cross-reacted with other serotypes.

Of the 43 individuals who provided paired serum specimens, 42 were available for answering questionnaires. Ten individuals had an illness in the last year compatible with an icteric leptospirosis. Illnesses were usually mild and nonspecific, with the most frequent complaints being fever, headache, conjunctivitis, photophobia, chills, stiff neck, rash, nausea, and vomiting. Only 5 of these 10 had at least a significant ($\geq$ 1:100) titer to leptospirosis, and only 3 had a fourfold change in titer. Among the 32 individuals who reported no illness compatible with leptospirosis in the last year, 7 had significant titers and 5 had fourfold titer changes. By Fisher's Exact Test, there was no significant difference in terms of serologic reactions between persons reporting illness and those who had not been ill.

Virtually all individuals reported that they had seen rats and mongooses in the neighborhood and that rats frequently entered the house. Contact with domestic animals, especially dogs, chickens, and pigs, was reported by the majority of those interviewed, but reported animal contact bore no relationship to serologic reactivity. Butchering of chickens, pigs, and rabbits was also common and was reported by significantly more ($p < .05$) individuals over 15 years of age (62 percent) than under that age (23 percent). All the children, but only a few of the adults, admitted having contact with the stream which had been suspected as the source of the deceased girl's infection. This reflected the fact that swimming and playing in the water were children's pastimes. Since most of the children had negative titers to leptospirosis, there was no relationship between serologic reactivity and contact with the stream.

Domestic Animals

The farm cows grazed in the pasture on both sides of the suspected stream. Isolations were made from the urine of three of the four cows, and later these isolates were identified as *pomona* by the agglutination-absorption technique. However, no leptospires were identified by fluorescent antibody staining of the urine sediment. All blood cultures from the cows were negative for leptospires. Although there were serologic reactions in three of five of the cows, the titers were low ($<$ 1:100) and reactions were in the *icterohaemorrhagiae* serogroup. Such reactions can occur because of paradoxical cross-patterns. One of the culture-positive animals was sero-negative, which is also not unusual.

Of the two dogs that were bled, the farm dog was negative; but the pet with a past history of jaundice had a titer of 1:1600 to *icterohaemorrhagiae*, which was indicative of infection with leptospirosis.

TABLE II
LEPTOSPIRE CULTURE AND SEROLOGY RESULTS
RATTUS SP.

Rat	Blood	Urine	Brain	Kidney		Serology	Serotype on Cultured Isolates Two-Way Absorption
1	—	—	—	+*	1:400 1:50	*icterohaemorrhagiae* *mankarso*	*icterohaemorrhagiae*
2	+*	+*	—	—	NR		*icterohaemorrhagiae*
3	—	+*	—	+*	1:3200 1:800	*icterohaemorrhagiae* *mankarso*	*pomona*
4	+*	ND	—	—	1:200	*icterohaemorrhagiae*	*icterohaemorrhagiae*
5	—	—	+*	—	NR		*icterohaemorrhagiae*
6	—	—	—	—	1:100 1:50	*icterohaemorrhagiae* *mankarso*	
7	—	+*	—	—	1:100 1:200	*icterohaemorrhagiae* *tarassovi*	*icterohaemorrhagiae*
8	—	+	+	+*	1:200	*tarassovi*	*icterohaemorrhagiae*
9	—	ND	—	—	NR		
10	ND	+*	—	—	ND		*icterohaemorrhagiae*
11	—	—	—	—	NR		

ND -- Not Done

NR -- Nonreactive

** - Refers to specimen or tissue on which serotype was identified.*

Wild Rodents

Fourteen *Rattus* sp. (probably *Rattus rattus)* were captured, but three died before reaching the laboratory. Results from cultures and serology in the remaining 11 are presented in Table 2. Leptospires were isolated from at least one body fluid or organ in eight of them. Seven were identified as *icterohaemorrhagiae* and one as *pomona* by two-way absorption with the MA test. The fact that two of these animals had positive blood cultures indicates that these animals were probably in the acute septicemic stage of the infection.

Discussion

Leptospirosis is not always appreciated as the widespread rather common infection that it is (2). Many clinicians still incorrectly think of leptospirosis as synonymous with its severe form, Weil's Disease. Because the clinical manifestations of the infection are so varied and are frequently very mild or unrecognized, it is often mistaken for other infectious diseases (2, 4). For this reason, confirmation of the diagnosis must rest on isolation of the organism and serologic testing and

not on clinical impression alone. Diagnosis depends on the physician's awareness of the local epidemiology of leptospirosis and a high index of suspicion.

This report presents data on the occurrence of leptospirosis in one area of semi-rural suburban San Juan. As in many other places where the infection is apparently rare, an index case or even a suspected index case led to evidence of the rather widespread distribution of leptospirosis in man and domestic and wild animals (4). In this report the diagnosis of leptospirosis in the "index case" could not be confirmed by laboratory methods in her 6-day clinical course. There are no confirmatory tests that will detect antibody before 7 days after the onset of illness. For this reason, details of her case were not presented. Clinical aspects of leptospirosis have been reviewed in detail recently by Feigen and Anderson (1).

The semi-rural environment in which this investigation took place is ideal for the maintenance of leptospirosis. Heavy tropical foliage keeps much of the neighborhood shaded and moist from the frequent rains and high humidity. Along with this moisture, warm temperatures provide good conditions for the survival of the leptospires in the free state (2). It is interesting to note that this survey took place in August, when there was a period of heavy rainfall in the San Juan area. The association of rainfall with leptospirosis in Puerto Rico has been noted previously (14), and the seasonal occurrence of cases in the early fall has been seen with some regularity in the United States for the last decade (15).

As in many areas of rural Puerto Rico, the practice of keeping domestic pigs and chickens in back yards was very common in the area investigated, and food for these animals was readily available to a large rat population. As noted above, rats were frequently seen entering the houses, and the opportunity for contamination of foodstuffs and food preparation surfaces with urine must have been common. Entry of virulent leptospires through the broken or abrased skin or through broken mucous membranes of the human population could easily follow. Rats captured in the immediate neighborhood were frequently infected with leptospires of serotype *icterohaemorrhagiae* (58 percent). Five of the eight individuals with significant titer change reacted within the *icterohaemorrhagiae* serogroup. *Bataviae*, the other common serum reaction identified in humans in this investigation, has previously been identified serologically from rats in Puerto Rico (9), but serologïes in rats are not reliable.

One dog in the neighborhood had an icteric illness characteristic of leptospirosis several months before this investigation, and its sera reacted strongly to *icterohaemorrhagiae*. This dog apparently had not been immunized, but it has been shown that where leptospire infection in rats is prevalent, even healthy-appearing, immunized dogs can become infected and shed leptospires in their urine (18).

The possibility that infection of the deceased girl and her neighbors resulted from exposure in the swimming hole is supported by the fact that cows grazed in the surrounding pasture and dogs also frequented the area. Previous outbreaks of swimming hole leptospirosis are well documented (19-21). The fact that the cows reacted to *pomona* and no human sera reacted in this serogroup is not incompatible with the cows being a source of infection. Paradoxical serologic cross-reactions can occur, and serologies alone are not reliable in identifying the offending organism. Unfortunately, no attempt was made to actually isolate leptospires from the stream, and it should be noted that only one of the 33 individuals under 30 (these were the persons potentially most heavily exposed to organisms in the stream) had a significant serologic reaction.

Another possible source of human infection in this population was the intimate contact with domestic animals during butchering. The occupational hazard of leptospirosis in abattoir workers has long been recognized (2, 4), and both swine and chickens are known carriers and shedders of leptospires (2, 3). In the group studied in this report, essentially only adults over 30 had significant serologic evidence of infection, and it is also the adults which more commonly reported butchering chickens and pigs. As in cows, the type of leptospire usually found in swine is *pomona*. Although this was not the serogroup to which the people reacted, swine could have been a source and paradoxical serologic reactions may have occurred. It is important to point out that leptospirosis should no longer be considered solely an occupational disease. Reports indicate that most cases in recent decades have occurred as a result of household contacts and recreational activities (1). The pattern of seroreactivity in the group studied here is compatible with this finding.

The limitations of this brief study do not allow us to make any statement about the age, sex, or overall prevalence of serologic positivity to leptospirosis in this community because no population denominator was defined and the sample of people studied was not randomly selected. The fact that the age of most of the

individuals with reactive serologies was over 40 does not agree with the peak prevalence of cases in the 20- to 30-year age group reported by Alexander (14), perhaps because of the non-representative nature of the sample studied. Comparison of the prevalence of positive reactors in this population with that of other normal populations has to be made cautiously because of differences in laboratory technique and criteria of positivity. However, the frequency of significant titers (28 percent) and even significant titer changes (19 percent) in the study population was higher than the 13.9 percent of 1931 sera reported positive (≥1:100) by Alexander *et al* (14) in their island-wide survey. The level of reactivity was much higher than the 2.6 percent prevalence noted in a survey of 1,077 unselected hospital admissions in Missouri where a more liberal definition of positive reaction (≥ 1:50) was used. In Thailand (a country with climatic conditions roughly comparable to those of Puerto Rico) there was, however, a 22-35 percent prevalence of positive reactors (≥ 1:100) in 3,746 nonfebrile hospital patients (22). The two most common serotypes identified were the same as those from cases reported by Alexander *et al* (14) where out of 73 isolates, 75 percent were *icterohaemorrhagiae* and 10 percent were *bataviae*.

The frequency with which isolates were obtained from rats in this study (67 percent) was striking, but not unusual. Leptospires can be isolated from 27-45 percent of urban rat species (23), and 32 percent of 104 rats trapped in Puerto Rico were reported positive by Alexander *et al* (14).

Also the isolation of leptospires of serotype *pomona* from rats is not unusual. Turner (2) has emphasized that although a particular animal species serves as a reservoir of only specific serotypes, it can also be infected with other serotypes and act as an incidental temporary host for those serotypes.

The frequent subclinical nature of infection with leptospires has now been documented by several serologic surveys (22, 24). The population of Barrio Santa Rosa was no exception. It is quite possible, however, that because questions about recent illness covered the previous year, some of those who reported compatible illnesses during that time could have become seronegative by the time of the survey. There is no question that leptospires were present in this environment and opportunities for infection and disease were many.

The laboratory diagnosis of leptospirosis is not difficult. The isolation of organisms by culture in semi-solid medium is the most reliable method, but success of the method depends upon prompt inoculation of specimens into media. Since excess amounts of blood or urine can inhibit growth of leptospires, serial dilutions of urine and serial increasing amounts of blood (i.e., 1 drop in 1st tube. 2 drops in 2nd tube, 3 drops in 3rd tube) are advised.

Serologic testing is most accurate when performed on paired acute and convalescent sera taken 2-3 weeks apart. The macroscopic-agglutination (slide) test (ST) is the best for rapid screening in general laboratories, but the MA which uses live antigen is preferable in terms of specificity. Details on how specimens should be collected and handled for both isolation and serology are available in several publications (1, 16). Because of the complexities of the diagnostic tests and the expertise required to run them, it is recommended that specimens be sent to laboratories where culture and serologic tests for leptospirosis are done routinely (1). The standard reference laboratory is the FAO/WHO Collaborating Center for the Epidemiology of Leptospirosis at the Center for Disease Control in Atlanta, Georgia.

Physicians need to be continually aware that the combination of climatic conditions, suitable rat habitats, human behavior, and the endemicity of leptospires in Puerto Rico make it likely that leptospirosis will be a frequent cause of otherwise unexplained febrile illness. Cases of viral meningitis and encephalitis should especially arouse suspicion of a leptospiral etiology. Finally it should be obvious that the information presented in this report may represent only the tip of the iceberg, and further epidemiologic studies of leptospirosis on the island, backed up by modern laboratory capabilities, should be attempted.

Summary

Leptospirosis was suspected as the cause of a fatal illness in a 10-year-old female patient from a rural barrio of Guaynabo. An investigation was conducted to detect the source of the infection and possible other cases among her neighbors. Twelve of 43 individuals (28 percent) who gave paired sera samples 3 weeks apart had significant titers (≥ 1:100) to leptospirosis, and 8 (19 percent) had a fourfold or greater change in titer diagnostic of recent infection. Seven of these 8 were adults over 30 years of age. The predominant serotypes were *icterohaemorrhagiae* and *bataviae*. Although 10 of 42 persons (23 percent) interviewed had an illness com-

patible with leptospirosis in the previous year, there was no observed statistical relationship between illness and serologic reactivity. Most of the individuals who cooperated by giving blood had been swimming with the "index case" in a stream located in pasture where domestic cattle grazed. Urine from 3 of 4 of these cattle produced leptospires of the serotype *pomona*. Eight of 11 rats captured from the neighborhood where the girl lived were infected with *icterohaemorrhagiae*. Serum from one canine house pet with a recent history of an icteric illness was strongly reactive to *icterohaemorrhagiae*. Although the clinical impression that the deceased girl had leptospirosis was never documented by laboratory evidence or autopsy, this survey provided abundant evidence that leptospira were present in the area where she lived. Despite its frequent subclinical nature, leptospirosis is probably a much more frequent cause of mild febrile illnesses, fevers of unknown origin, and aseptic meningitis than is currently appreciated, and the possibility of severe disease is always present.

Acknowledgments

Dr. Raúl H. López-Correa, Instructor in Pediatrics and Infectious Diseases at University District Hospital, San Juan, was responsible for the care and investigation of the suspected case and assisted in the survey of the human population. The Vector Control Division of the Puerto Rico Health Department kindly provided traps and technical assistance in capturing rats. We also wish to thank Wilda B. Knight, Luis Rivera Báez, and Rafael Hernández Colón of the San Juan Laboratories for their assistance in obtaining the specimens.

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VITAMIN B_6 INTAKE AND URINARY EXCRETION OF 4-PYRIDOXIC ACID PER GRAM OF CREATININE IN A RURAL PUERTO RICAN AREA

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A nutrition survey was carried out in the rural area of Duey Alto, San Germán, Puerto Rico, during March 1964. The survey included the collection of clinical, biochemical, and dietary data. The dietary survey included a group of representative families and was done using the 24 hour individual weighed intake method. Urinary excretion rates of thiamine, riboflavin, N'methylnicotinamide, and 4-pyridoxic acid per gram of creatinine were determined in casual urine specimens.

The results of this survey were published in 1967 (1). However, the ingestion of Vitamin B_6, the urinary excretion of 4-pyridoxic acid, and their interrelation were never analyzed and published. It is, therefore, the purpose of this work to reveal such data, and to discuss its relevance in regard to the B_6 nutritional status of our rural dwellers.

Methods

The study included 38 subjects belonging to 15 representative families. Families were selected according to size, annual income, and geographic distribution within the rural community. The exact food intake of each individual was weighed for one 24 hour period by a dietary team. Food consumption was obtained by the recipe method. The ingredients entering in the composition of each dish were weighed separately as well as the final cooked dish. Individual portions and leftovers were also weighed. Pyridoxine consumption was calculated using food composition tables (2, 3, 4).

Urinary excretion rates of 4-pyridoxic acid per gram of creatinine were done in casual urine specimens. 4-pyridoxic acid was determined by the following procedure: 8 ml. of a dilution of 1 ml. of urine in 100 ml. of ionized water was placed in a cuvette and the pH was adjusted to 8 with the addition of sodium borate using Hydrion pH paper. Reading was done with setting at 100 using a Coleman photofluorometer. Quinine standard was used for setting. This procedure was a very simple one developed by the Army Tropical Research Laboratories at San Juan, Puerto Rico. The amount of creatinine was determined by the Jaffe reaction (5).

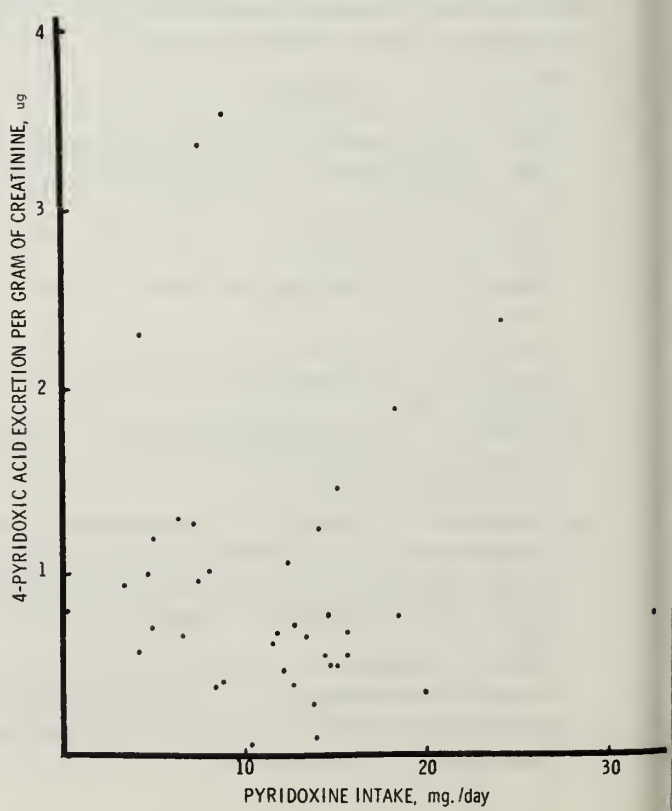
The dietary intake and the urine specimens were not always obtained during the same day. However, all the data was collected within a period of 6 days.

Results and Comments

The results of the study are summarized in Tables I, II, III, and Diagram 1.

Table I shows the average B_6 intake by age group and sex. The mean intake and all the individual

DIAGRAM 1: CORRELATION BETWEEN B_6 INTAKE AND 4-PYRIDOXIC ACID EXCRETION PER GRAM OF CREATININE



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This study was supported by Grant AM-06032 from the National Institutes of Health to the Dept. of Biochemistry and Nutrition, School of Medicine, University of Puerto Rico.

TABLE I: AVERAGE DAILY B_6 INTAKE BY AGE GROUP AND SEX

Age Group	4 - 6	7 - 10	11 - 14	15 - 18	19 - 50		>50		All Ages
SEX	MF	MF	MF	MF	M	F	M	F	MF
NO.	3	6	4	3	8	7	3	4	38
MEAN B_6 INTAKE, mg.	11.7	8.1	12.0	9.5	13.9	10.2	14.9	8.4	11.1
RECOMMENDED ALLOWANCE mg.	0.9	1.2	1.6	1.9	2.0	2.0	2.0	2.0	1.7

TABLE II: MEAN DAILY B_6 PROVIDED TO THE SAMPLE OF 38 SUBJECTS STUDIED BY EACH INDIVIDUAL FOOD AND BY FOOD GROUPS (mg)

1. MILK AND PRODUCTS:		
	Fresh	9.19
	Evaporated	0.96
	Dry Whole	0.50
	Dry Skim	0.26
	American Cheese	0.53
	Total -	11.44
2. MEAT, FISH, AND EGGS:		
	Cured Ham	17.69
	Fresh Beef	15.75
	Corned Beef	11.38
	Pork	3.55
	Salami	1.89
	Vienna Sausage	1.40
	Codfish	3.56
	Eggs	7.10
	Total -	62.32
3. LEGUMES:		
	Red Kidney Beans (rosita)	54.37
	Pigeon Peas	22.55
	Red Kidney Beans (Large)	14.99
	White Navy Beans	10.96
	Total -	102.87
4. STARCHY VEGETABLES:		
	Potatoes	35.79
	Green Bananas	34.08
	Yam	14.62
	Plantain	3.01
	Tanier	2.51
	Dasheen	1.86
	Total -	91.87

5. OTHER VEGETABLES:		
	Pumpkin	3.74
	Lettuce	3.20
	Vegetable Soup	2.43
	Tomato	0.69
	Total -	10.06
6. FRUITS:		
	Banana	35.33
	Orange	7.70
	Soursop	2.38
	Custard Apple	1.87
	Total -	47.28
7. CEREAL PRODUCTS:		
	Rice	61.29
	Whole Corn	9.76
	Bread	5.20
	Soda Crackers	1.14
	Cornmeal	0.77
	Noodles	0.77
	Macarroni	0.68
	Total -	79.61
8. SWEETS AND DESSERTS:		
	Cookies	0.86
	Sugar Cane	0.40
	Cake	0.38
	Papau (sweet)	0.16
	Chocolate candy	0.15
	Gelatin	0.07
	Total -	2.02
9. SAUCES AND SPREADS:		
	Tomato Sauce	13.57
	Sandwich Spread	0.03
	Total -	13.60

ingestions were above the daily recommended dietary allowances (6). Only one subject whose diet was well below normal did not fulfill the recommendation. Among adults, males showed higher average ingestions than females.

The mean daily amount of pyridoxine provided to the sample of 38 subjects by each individual food and by food groups is detailed in Table II. Within each group, the foods are listed in order of the amount of B_6 provided.

Individually, rice was the highest provider of pyridoxine. As a group, the legumes, particularly red kidney beans (rosita variety), accounted for the highest intake. The proportion provided by each food group was the following: legumes 24.4 percent; starchy vegetables 21.8 percent; cereal products 18.9 percent; meat, fish and eggs 14.8 percent; fruits 11.2 percent; sauces and spreads 3.2 percent; milk and products 2.9 percent; non-starchy vegetables 2.4 percent; and sweets and desserts 0.5 percent.

From the above data it is clear that the dietary ingestion of B_6 was very adequate, and that two of our staple foods, rice and red kidney beans, were excellent sources of the vitamin.

Table III and Diagram 1 demonstrate the correlation observed between the ingestion of vitamin B_6 and the urinary excretion of 4-pyridoxic acid per gram of creatinine. According to Sauberlich information is not available as to whether or not random urine samples could be employed with the 4-pyridoxic acid levels related to creatinine excretion in the assessment of B_6 nutritional status in man (7). Our data, therefore, could represent the first published information in this respect.

TABLE III: INDIVIDUAL B_6 INTAKE AND 4-PYRIDOXIC ACID EXCRETION

Subject	Age	Sex	B_6 Intake (mg)	4-pyridoxic acid excretion (ug/gm)
1. A. R.	3	F	4.1	0.58
2. A. E.	4	F	12.6	0.38
3. C. E.	5	F	18.3	1.09
4. W. R.	7	M	7.1	1.27
5. N. R.	9	F	12.6	0.71
6. D. A.	9	F	8.8	3.54
7. C. R.	10	M	7.4	0.96
8. G. R.	10	F	4.9	1.21
9. J. C.	10	M	8.4	0.38
10. E. A.	11	F	8.8	0.40
11. T. R.	11	F	14.8	0.48
12. V. R.	12	F	10.5	0.48
13. O. A.	13	F	13.8	0.27
14. C. R.	16	F	6.6	0.64
15. R. O.	16	F	6.2	1.31
16. C. C.	16	F	15.6	0.66
17. F. A.	19	M	19.9	0.32
18. L. P.	22	F (L)	13.8	0.09
19. S. O.	23	M	7.5	3.38
20. J. C.	23	M	13.2	0.65
21. A. O.	26	F	14.7	1.50
22. E. T.	29	M	11.5	0.61
23. R. J.	33	F	4.1	2.32
24. L. E.	34	M	0.0	0.80
25. M. R.	38	F	3.3	0.93
26. E. R.	40	M	32.6	0.87
27. A. L.	45	F	12.2	1.06
28. C. T.	45	F	12.0	0.44
29. S. E.	46	M	7.9	1.01
30. V. A.	48	M	18.3	0.75
31. M. I.	50	F	11.6	0.66
32. P. E.	57	F	10.1	0.03
33. L. I.	58	M	15.6	0.52
34. P. O.	59	M	14.4	0.53
35. E. A.	63	F	4.9	0.70
36. M. M.	65	F	4.5	1.00
37. A. M.	70	F	14.0	1.23
38. J. R.	72	M	14.6	0.75

L – lactating female

As a whole, a very poor association was observed in our study between pyridoxine intake and 4-pyridoxic acid excretion per gram of creatinine. Only 9 subjects or 24 percent of the sample studied showed a satisfactory linear correlation. The values plotted in Diagram 1 confirm the previous statement. Nevertheless, the correlation coefficient between the values of the two variables, as presented in Table III, was calculated in order to further assess any possible degree of association between them. The correlation coefficient was -0.23, showing that only 5.3 percent of the changes observed in B_6 ingestion could account for the corresponding urinary excretion values of 4-pyridoxic acid per gram of creatinine.

We are perfectly aware of the limitation of the method utilized by us in the determination of 4-pyridoxic acid in urine. pH fluorescence curves show that in normal urines substances other than 4-pyridoxic acid may be measured by the method, and thus higher values erroneously obtained for 4-pyridoxic acid excretion (8). However, if 4-pyridoxic acid excretion per gram of creatinine in casual urine specimens could

be possibly used as a practical means of determining nutritional status with respect to this vitamin, a much better direct correlation would have been necessary. The simplicity of the method made it practical for field studies, but the lack of association observed with B_6 ingestion is definitively against it as a reliable field procedure.

Summary

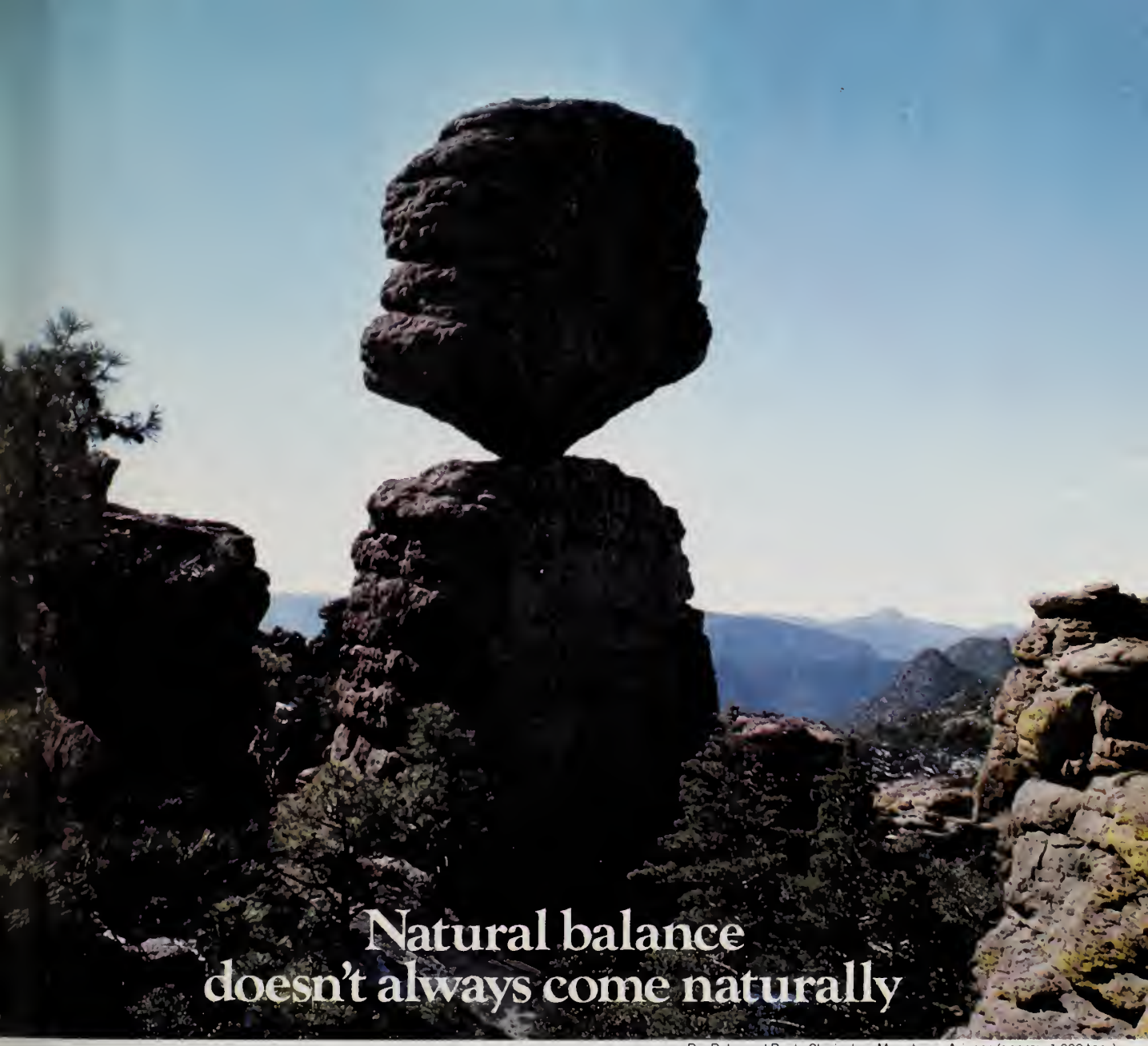
A nutrition survey was carried out in a rural Puerto Rican community in which dietary, clinical and biochemical data was collected. In this paper the ingestion of vitamin B_6 and its relation to the urinary excretion of 4-pyridoxic acid per gram of creatinine in random urine samples is discussed. The data reveal that the ingestion of vitamin B_6 was very adequate. Rice and red-kidney beans were the principal dietary sources. A very poor statistical association between pyridoxine intake and 4-pyridoxic acid urinary excretion per gram of creatinine was observed.

Resumen

Una encuesta nutricional fue realizada en un área rural de Puerto Rico. Se obtuvieron datos dietéticos, clínicos y bioquímicos. En este trabajo se discute la ingesta de vitamina B_6 y su relación con la excreción urinaria de ácido 4-piridóxico por gramo de creatinina en muestras casuales de orina. Los resultados revelan que la ingestión de piridoxina fue muy adecuada siendo el arroz y las habichuelas coloradas las principales fuentes dietarias de ésta. Una relación estadística muy pobre fue encontrada entre la ingesta de vitamina B_6 y la excreción urinaria de ácido 4-piridóxico por gramo de creatinina.

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Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo.*
- Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

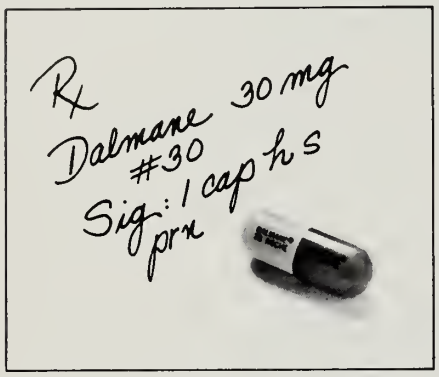
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Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ



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RECENT ADVANCES IN EXTERNAL PULSE RECORDINGS

Juan M. Aranda, MD
Benjamín Befeler, MD, FACC

To the physician skilled in auscultation, the phonocardiogram is useful to confirm his auscultatory findings and to furnish precise timing of the audible events. To accomplish this, it is very useful to record the phonocardiogram simultaneously with the apexcardiogram, the carotid pulse or jugular pulse tracing.

External pulse recording is not a substitute for the ear or the hand. Although many murmurs and sounds can be characterized by phonocardiography, this technique occasionally fails to register certain sounds such as the high pitched diastolic murmur of aortic insufficiency. However, when the technique is properly used, it makes possible the accurate timing of events which may be too rapid or too subtle to be discerned by our senses.

Figure 1 shows the phonocardiogram carotid pulse tracing and apexcardiogram of a 25-year old male subject with a systolic click and a late systolic murmur. The following values and relationships are noted (1):

1. The first heart sound (S_1) lasts from .10 to .12 sec.
2. The second heart sound (S_2) is normally split up to .08 - .10 sec on inspiration and up to .04 sec on held expiration.
3. S_1 is composed of four major elements (1):
   a. Low frequency vibrations which coincide with the beginning of left ventricular contraction and are probably caused by muscular contraction at the onset of left ventricular systole.
   b. Higher frequency vibrations which represent mitral valve closure and comprise the major component of the first heart sound, however, at the present time there is disagreement whether acute valve closure produces sound or is silent. It begins .02 sec after the onset of the first component.
   c. High frequency vibrations which follow mitral valve closure by .03 second. It is believed that they are associated with the beginning of ejection into the great vessels. Recent observations favor the concept that closure of the tricuspid valve is responsible for this component (2).
   d. Acceleration of blood into the great vessels produce low frequency vibrations which account for the fourth component of S_1.
4. The third heard sound is a low frequency sound which occurs during the rapid ventricular filling phase. It is probably secondary to the abrupt tensing of the chordae tendinae and valve leaflets within the left ventricular cavity. It occurs at an average of .15 second after aortic valve closure (.10 - .24 sec). It lasts from .04 to .05 sec and coincides with the rapid filling phase of the apexcardiogram and the y descent of the jugular pulse tracing.
5. The fourth heart sound (S_4) begins about .12 to .17 sec after the onset of the p wave. It coincides with the a wave of the jugular pulse tracing and the late filling phase (A wave) of the apexcardiogram. It is recorded in the phonocardiogram even when it is impossible to hear. It is believed to be produced by vibrations set up within the mitral valve apparatus (leaflets and chordae) as the ventricles expand with the inflow of blood produced by atrial contraction. It begins before the onset of the QRS complex. This helps to distinguish it from the early component of the first heart sound.

The phonocardiogram is helpful in assessing objectively the response of murmurs and clicks to different physiologic maneuvers and drugs. Through this technique, it has been documented that systolic clicks arising from the mitral valve apparatus move closer to

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S_1 in the upright position or after amyl nitrite (1). In other words, if an early or midsystolic click moves closer to the first heart sound in the upright position or after inhalation of amyl nitrite, it is of mitral origin. Ejection clicks arising from the aortic valve or from a dilated ascending aorta do not behave in this fashion. Serial phonocardiographic tracings are of unlimited value in detecting dysfunction of aortic or mitral valve prosthesis. Changes in the intensity or absence of prosthetic valve sounds are usually an ominous sign of impending malfunction. A prolonged interval from aortic valve closure (A_2) to the opening click of a prosthetic mitral valve suggests an impediment to movement of the ball or disk valve, usually a thrombus. In patients with aortic prosthetic valves, an aortic opening click-closing click height ratio of less than .5 is consistent with ball variance (3-5).

Carotid Pulse

The carotid pulse represents a direct pipeline from the left ventricular cavity. Its contour reflects the hemodynamics of left ventricular ejection and the function of the aortic valve (6). The carotid pulse tracing is very useful in detecting the aortic component of the second heart sound, which occurs .01 to .03 sec before the dicrotic notch (2) (Figure 1). This relationship tends to remain constant in the same individual. On the other hand, the pulmonic component of the second heart sound may fall before, during or after the dicrotic notch, varying its relationship with respiration. The carotid pulse is also very helpful to differentiate between aortic stenosis and idiopathic hypertrophic subaortic stenosis (7). The carotid pulse normally begins to rise abruptly with aortic ejection and reaches its initial peak at the time that ejection is maximal. Obstruction of blood flow across the aortic valve results in prolongation of ventricular ejec-

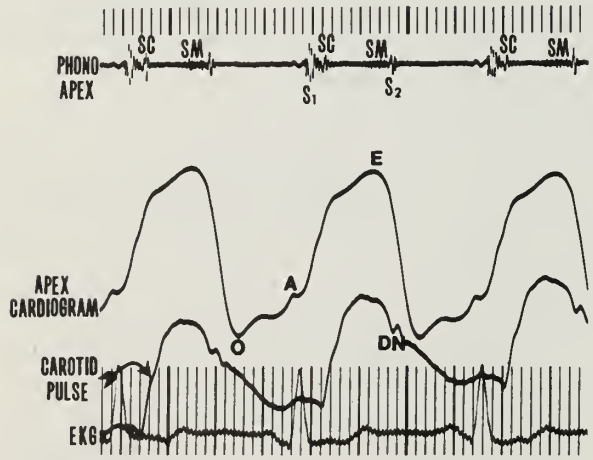


Figure 1: *Simultaneous recording of the phonocardiogram, apexcardiogram, carotid pulse and electrocardiogram in a patient with a systolic click and a late systolic murmur. Note the time relationship between the heart sounds and the pulsatile events. S_4 coincides with the A wave of the apexcardiogram. The steep rise of the apexcardiogram occurs with or shortly after the first component of S_1. The dicrotic notch of the carotid pulse (DN) occurs about .01 to .03 sec after A_2.*

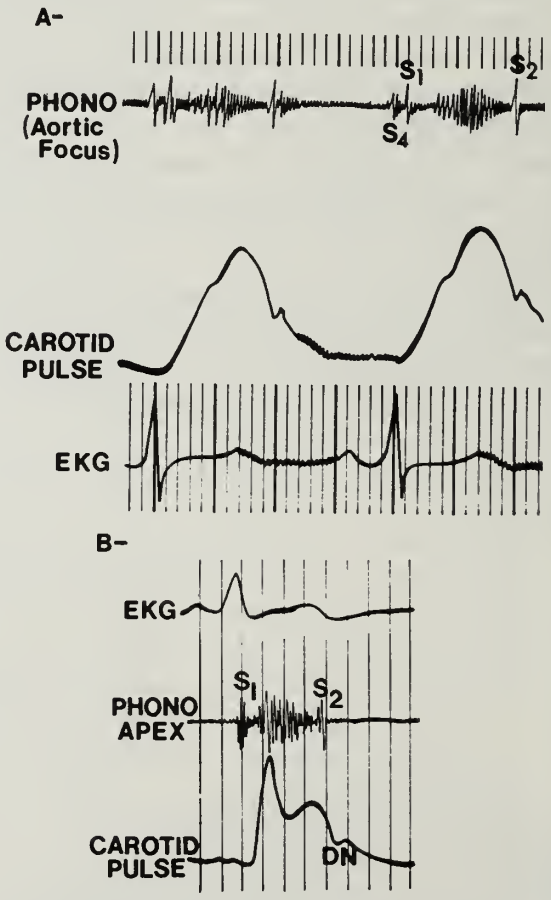


Figure 2: *A) Carotid pulse recording in a patient with severe aortic stenosis. Note the slurred and delayed upstroke of the carotid pulse. The rate of rise of the carotid pulse was 325 MM Hg/sec. B) In patients with IHSS the upstroke of the carotid pulse is sharp and rapid followed by a late systolic plateau and a bifid pulse. The rate of rise of the carotid pulse was 825 MM Hg/sec, but the LVET was prolonged.*

tion. As a result, the carotid pulse tracing will show an abnormally slow initial upstroke and a prolongation of total ejection time (Figure 2). The maximal rate of rise of the arterial pulse calculated from the carotid pulse tracing, the left ventricular ejection time (LVET) and the time interval between the Q wave of the EKG to the peak intensity of the aortic murmur have been correlated with the severity of aortic stenosis (7). As the systolic gradient across the aortic valve increases, the rate of rise of the carotid pulse decreases, the LVET increases and the interval between the Q wave of the EKG to peak intensity of the murmur increases. A rate of rise of the carotid pulse less than 500 mm Hg/sec, a LVET > .42 sec and a Q-peak intensity interval > .19 sec indicate severe aortic stenosis (> 75 mm Hg systolic gradient). In patients with idiopathic hypertrophic subaortic stenosis, the carotid pulse has a rapid upstroke followed by a mid to late systolic plateau (Figure 2). As a result, the rate of rise of the carotid pulse is normal but the LVET is prolonged. These graphic findings reflect the fact that obstruction occurs only after the onset of left ventricular systole when there is systolic anterior movement of the anterior leaflet of the mitral valve toward the thickened interventricular septum.

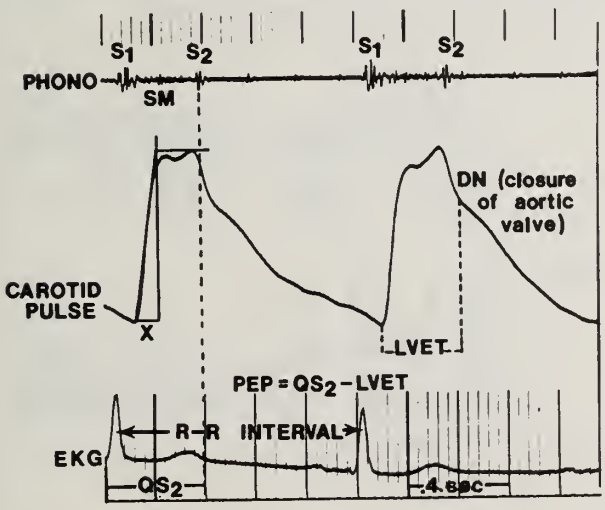


Figure 3: *Simultaneous recording of the phonocardiogram, carotid pulse and electrocardiogram in a 40 year old male with an aortic ejection murmur. X represents the time required to reach the maximum peak of the carotid pulse. Dividing the pulse pressure by X provides an approximate value of the rate of rise of the carotid pulse (normal value, 600 - 900 MM Hg/sec).*

Systolic Time Intervals

Definitions (Figure 3)

1. Left ventricular ejection time (LVET) = Interval between the onset of the upstroke of the carotid pulse to the incisura (dicrotic notch).
2. Total electromechanical systole ($Q\text{-}S_2$) = Interval between the Q wave of the EKG to the aortic component of the second heart sound (S_2).
3. Pre-ejection period (PEP) = Interval between the Q wave of the EKG to the onset of the upstroke of the carotid pulse tracing. It can also be determined by substracting the LVET from the QS_2 interval (PEP = QS_2 - LVET). It is inversely related to changes in the inotropic state of the left ventricle.
4. PEP/LVET = This ratio is inversely related to the ejection fraction.

The measurement of systolic time intervals (STI) for the indirect assessment of cardiac function has been extensively documented (8, 9). Despite the fact that there are several determinants for each of these intervals, these measurements correlate well with more direct parameters of left ventricular performance.

In normal subjects the ejection time and duration of ventricular systole are dependent upon heart rate. As the rate increases, the ejection time, the PEP and the $Q\text{-}S_2$ interval shorten. Therefore, the heart rate must be taken into consideration in the calculation of the systolic time intervals. By using the following (8) formula, these intervals are corrected for heart rate and the obtained corrected values can be compared without taking into account the heart rate.

$$\text{Corrected value} = \frac{\text{Measured interval}}{\sqrt{\text{R-R interval (sec)}}}$$

The corrected values can also be compared to normal values previously reported (9).

Interval	Normal Corrected Value (sec)
LVET	.392± .022
PEP	.101± ,025
PEP/LVET	.257± .022

In the normal subject the LVET is predominantly influenced by stroke volume; at faster rates the stroke volume and the LVET are proportionally reduced (9).

Therefore, other factors remaining constant, the LVET is directly proportional to the stroke volume. The LVET is characteristically prolonged in patients with moderate to severe aortic stenosis and decreased in patients with congestive heart failure (Table I). Therefore, in patients with tight aortic stenosis and left ventricular dysfunction, the LVET and PEP are not clinically useful in assessing the severity of the lesion.

The PEP is the summation of electrical and mechanical events between the onset of electrical depolarization of the left ventricle and the opening of the aortic valve. It can be subdivided by the first heart sound into the QS_1 interval and isovolumetric systole (isovolumetric contraction time) (10).

The isovolumetric contraction time represents the time required by the ventricle starting at end diastole to generate sufficient pressure to open the aortic valve. Its determinants are left ventricular end diastolic pressure, the aortic diastolic pressure and the mean rate of left ventricular pressure development. Increased ventricular depolarization time, elevated aortic diastolic pressure and decreased rate of left ventricular pressure development prolong the PEP. This interval is characteristically prolonged in patients with congestive heart failure and shortened in patients with thyrotoxicosis (10). In the latter condition, the short PEP indicates a state of enhanced myocardial contractility. Short PEP can also be seen in aortic stenosis and insufficiency. As hyperthyroid patients become euthyroid the PEP significantly lengthens.

The PEP/LVET ratio tends to remain relatively constant in normal individuals. It usually magnifies minor changes in either component and bears a significant inverse relationship to left ventricular ejection time.

The Apexcardiogram

The apexcardiogram displays graphically the low frequency vibrations over the precordial area at the point of maximal impulse. The recording most frequently mirrors events in the normal individual caused predominantly by the left ventricle. The normal apexcardiogram (Figure 4) consists of an initial peak (E point) which corresponds to the ejection of blood from the left ventricle at the end of the isovolumic contraction period. The E point is followed by a rapid descent which levels off, reaching a plateau that ends before or at the time of S_2. The O point coincides with the opening of the mitral valve. With early rapid ventricular filling, the curve rises steeply giving rise to the rapid filling phase which coincides with the third heart sound (S_3). The A wave coincides with the late filling phase and the fourth heart sound (S_4).

FACTORS THAT DECREASE L V E T
1. - Decrease myocardial contractility
2. - Digoxin
3. - Hypercalcemia
5. - Decrease stroke volume
6. - Mitral insufficiency
7. - Rapid heart rate
8. - Thyrotoxicosis
FACTORS THAT INCREASE L V E T
1. - Enhanced myocardial contractility
2. - Increase stroke volume
3. - Increase afterload
4. - Aortic stenosis
5. - Aortic insufficiency

Table I

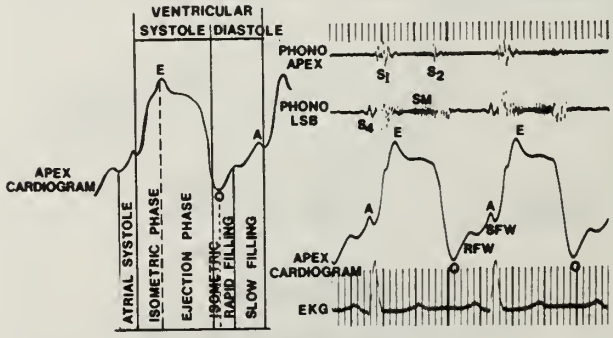


Figure 4: *Simultaneous phonocardiogram, apexcardiogram and EKG in a patient with papillary muscle dysfunction and ASHD. Note the S_4 and a mid-systolic murmur. A schematic representation of the various components of the apexcardiogram is shown. Note the rapid filling (RFW) and slow filling wave (SFW) as well as the A wave coinciding with the fourth heart sound.*

Note the following relations:

1. The steep rise of ventricular contraction occurs with the first component of S_1.
2. The E point occurs with or immediately after the third component of S_1.

The apexcardiogram is very useful in the differentiation between S_3 and OS. With increasing severity of mitral stenosis, there is greater elevation of left atrial pressure, the opening snap appears earlier in diastole thus shortening the A_2-OS interval. In cases of moderate mitral stenosis, the A_2-OS interval measures about .08 to .10 sec, if the interval is less than .06 seconds, the mitral pressure gradient is apt to be large and the stenosis severe (1).

Prominent A waves in the apexcardiogram usually indicate forceful and voluminous left atrial contraction arising in response to elevated left ventricular end diastolic pressure or decreased compliance of the left ventricular wall. In patients with clinical findings suggestive of aortic stenosis, a palpable apical "a" wave or an "A" wave height of greater than 10 percent of the total complex on the apexcardiogram is an important positive feature, suggesting severe aortic stenosis. However, its absence does not exclude severe valvular stenosis (11).

Jugular Venous Pulse

The jugular venous (Figure 5) pulse represents the hemodynamic events occurring in the right sided chambers. Conditions affecting the tricuspid valve, the right ventricle, the pulmonic valve and the pulmonary circulation may influence and modify the events in the right atrium.

The a wave of the jugular venous pulse is caused by right atrial contraction. The x descent caused by atrial relaxation begins with the downslope of the a wave.

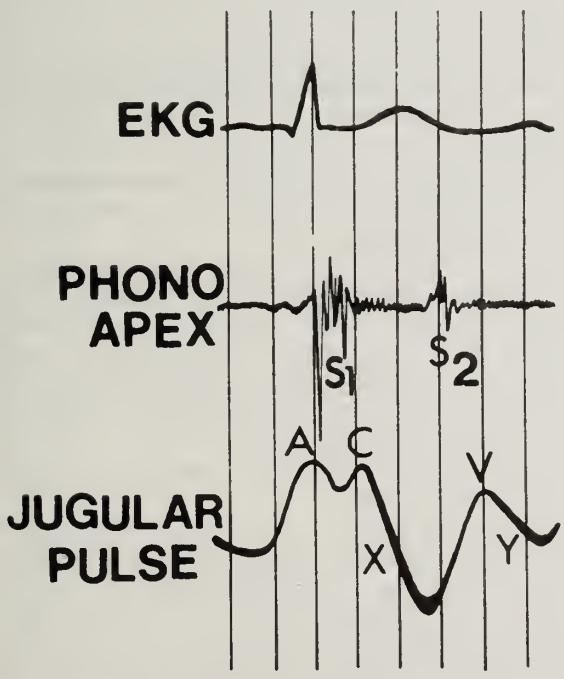


Figure 5: *Simultaneous electrocardiogram, phonocardiogram and normal jugular pulse tracing. The A wave is produced by atrial contraction. The X descent begins with the downslope of the A wave but is interrupted by the C wave. The V wave is secondary to right atrial filling with a closed tricuspid valve.*

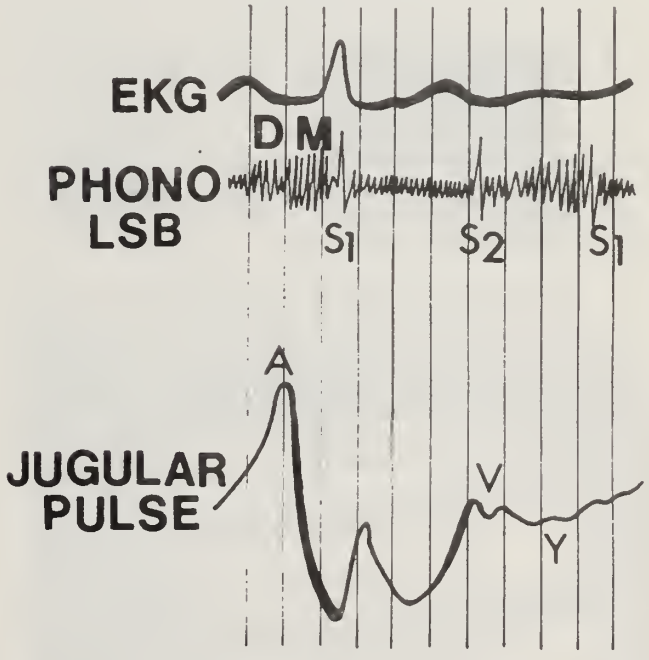


Figure 6: *Simultaneous electrocardiogram, phonocardiogram and jugular pulse recording in a patient with tricuspid stenosis. The jugular venous pulse shows a prominent A wave secondary to the increased force of contraction of the hypertrophic right atrium. The V waves are small and are followed by a plateau instead of the normal y descent, indicating inadequate opening of the tricuspid valve.*

It is interrupted by the c wave which is probably secondary to right ventricular contraction or tricuspid valve closure. The "v" wave follows and is caused by the inflow of blood into the right atrium with a closed tricuspid valve. The y descent begins with the opening of the tricuspid valve. Note that the "a" wave is normally the highest in the cycle and the x descent the lowest point. These events may be identified at the bedside by the following maneuvers; (a) on inspection, the largest negative wave is probably the x descent. (b) on palpation of the carotid pulse, the positive wave immediately preceding the carotid pulse is the "a" wave, the negative wave beginning at the moment of carotid impact is the x descent, the positive wave after the carotid pulse is the "v" wave, (c) on auscultation the positive wave preceding S_1 is the "a" wave, the positive wave following S_2 is the "v" wave.

When giant a waves are noted in the jugular venous pulse, systolic overloading of the right atrium is the hemodynamic mechanism responsible for this finding. This can be secondary to:

a. tricuspid stenosis (Figure 6)

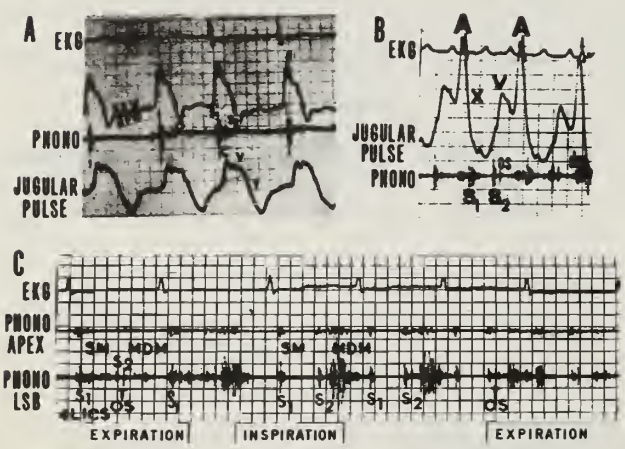


Figure 7: *Jugular pulse tracing in a patient with tricuspid insufficiency and atrial fibrillation. Prominent C-V waves are recorded followed by prominent Y descent. The X descent is completely obliterated by the V wave. A right ventricular apexcardiogram was also recorded. B) In tricuspid stenosis large A waves are recorded. The V waves are small and the Y descent is almost obliterated by the dominant A waves. Note the tricuspid opening snap and the late diastolic murmur. C) The murmur of tricuspid stenosis increases markedly with inspiration.*

b. pulmonic stenosis
c. pulmonary hypertension
d. right ventricular failure

Systolic pulsations indicate retrograde right ventricular ejection as found in tricuspid regurgitation (Figure 7). Prominent "v" waves indicate diastolic overloading of the right atrium. This is typically found in atrial septal defect, anomalous pulmonary venous drainage, tricuspid insufficiency and ruptured sinus of Valsalva into the right atrium. Absent venous pulsation is indicative of a block between heart and veins, tightly engorged veins as found in severe congestive heart failure, cardiac tamponade or obstruction of the superior vena cava. Kussmaul's sign or paradoxical venous filling with inspiration is usually seen in cases of congestive heart failure, restrictive diseases, obstruction of the superior vena cava, pulmonary embolism or bronchial asthma (6).

Acknowledgment

We express our appreciation to Miss Bonnie Agnell for the typewritten preparation of the manuscript.

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PROTESIS DE PENE "SMALL-CARRION". NUEVO SUPLANTE PARA EL TRATAMIENTO DE LA IMPOTENCIA

Michael P. Small, MD
Hernán M. Carrión, MD

Inspirados por los cirujanos plásticos en el desarrollo de una prótesis para implantación en los senos, la prótesis de pene Small-Carrión fue diseñada y desarrollada para pacientes a quienes las prótesis ya existentes resultaban ser inadecuadas. Un material de consistencia natural y más flexible, el cual no solamente le daría más longitud al "falo", sino más anchura y firmeza por igual, se logró combinando la forma de un exterior de silicona médicamente graduado con un interior de esponja de silicona. Este material fue desarrollado en cooperación con "The Heyer-Schulte Co." * y se encuentra disponible, exclusivamente, a través de ellos.

La idea de una prótesis apareada ha sido mantenida a un nivel de simplicidad básica.... eliminando cualquier innovación mecánica o hidráulica, mientras se incorporaban ciertas ventajas fisiológicas que ayudarían a eliminar algunos problemas encontrados con las prótesis hasta ahora existentes (1-8). Problemas, tales como expulsión, edema linfático, irritación del pene, dolor y dislocación de la prótesis, están prácticamente eliminados cuando esta nueva prótesis es implantada adecuadamente.

En combinación con la prótesis en sí, la técnica quirúrgica desarrollada y recomendada para su implantación ha previsto y evitado en casi su totalidad estas complicaciones, excepto en los casos más raros e infrecuentes. Quizás, por esta razón, el interés y la demanda por este implante ha sobrepasado todas nuestras expectaciones y los resultados han sido igualmente recompensados.

Hasta el momento como está disponible este implante --- en forma apareada --- parece tener todas las cualidades ideales deseables en prótesis de pene .... dando el adecuado ancho, longitud y consistencia más parecida a la del pene erecto. En forma apareada está disponible en cinco longitudes diferentes: 12 cm.; 13.3 cm.; 14.5 cm.; 15.8 cm. y 17.0 cm. y en dos diámetros: 0.9 cm y 1.1 cm (Figura 1). El tamaño apropiado de la prótesis es seleccionado en el momento de la operación. El diámetro menor es necesitado generalmente en pacientes en quienes se encuentra dificultad en dilatar el cuerpo cavernoso, como en aquellos que han tenido priapismo, enfermedad inflamatoria del cuerpo cavernoso, o extenso trauma del pene. La porción proximal de la prótesis es curva para ajuste y se acomode al crus del pene y es hecho de un material sólido de silicona médicamente graduado. La rigidez de la prótesis en esa área permite un soporte adecuado en el crus y tuberosidades isquial. Las prótesis en sí permiten ser esterilizadas en cualquier autoclave de hospital.

Para prevenir cicatrices en el pene, se recomienda acceso quirúrgico perineal. El paciente es colocado en posición de litotomía dorsal y se le coloca un cateter en la vejiga con propósito de orientación. Una incisión media, vertical, es hecha desde la base del escroto

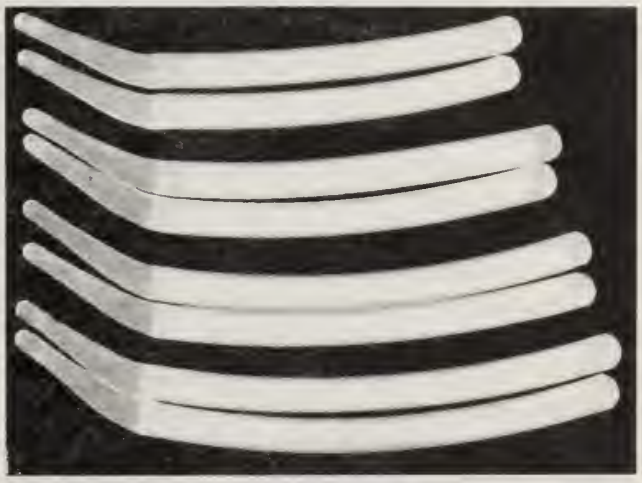


Figura 1

** - The Heyer-Schutte Corp. - Goleta, California, 93017.*

Del Departamento de Urología, Universidad de Miami, Escuela de Medicina.

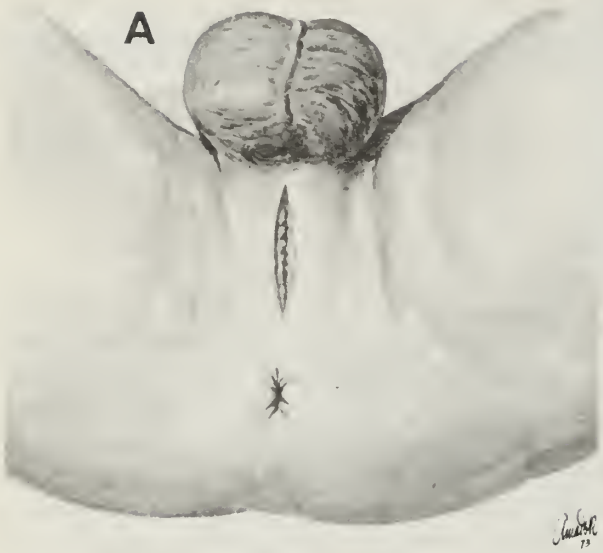


Figura 2

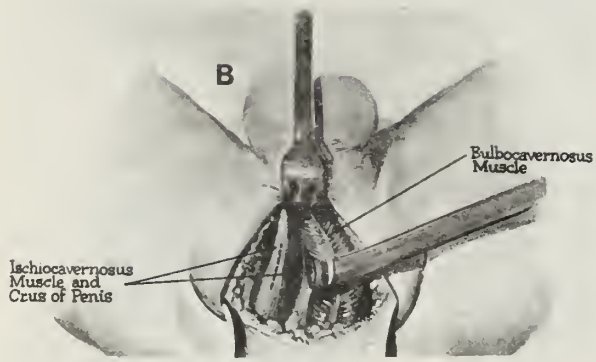


Figura 3

hacia el ano y llevada hasta el músculo bulbo-cavernoso (Figura 2). El bulbo-cavernoso y la uretra son retractados hacia un lado y el músculo isquial cavernoso y el crus del pene son identificados (Figura 3). Si se encuentra dificultad en identificar estas estructuras, una compresión firme del pene producirá un estímulo en el área del crus. Una vez que el crus ha sido identificado, se le abre con una longitud aproximada de dos centímetros. Entonces, dilatadores "Hegar" son usados para dilatar el crus del pene cerca de la tuberosidad isquial y distante de todo lo que comprende el cuerpo cavernoso (Figuras 4 y 5). Es imperativo que la dilatación sea llevada a cabo completamente hasta debajo del glande para que la prótesis encaje firmemente en esta área y no permita que el glande se doble sobre el implante. La dilatación generalmente se empieza con un dilatador "Hegar" número 5 y si no hay ningún tejido cicatrizal en el cuerpo

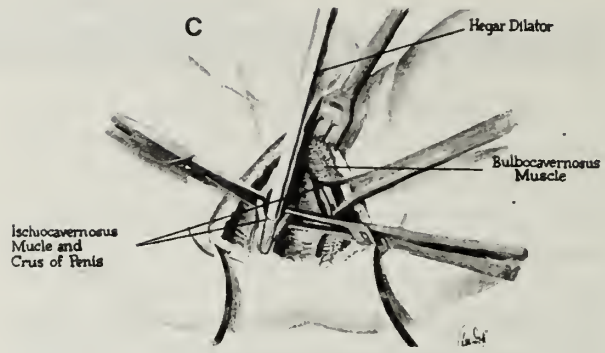


Figura 4

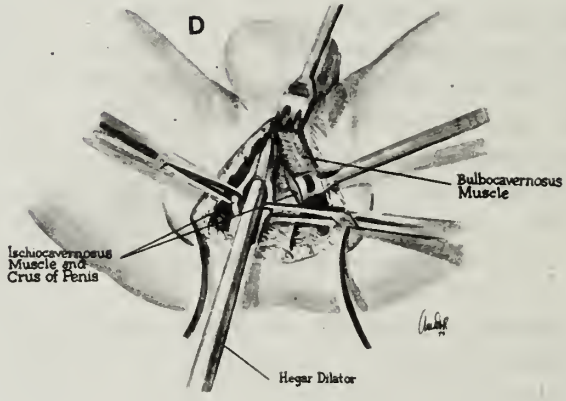


Figura 5

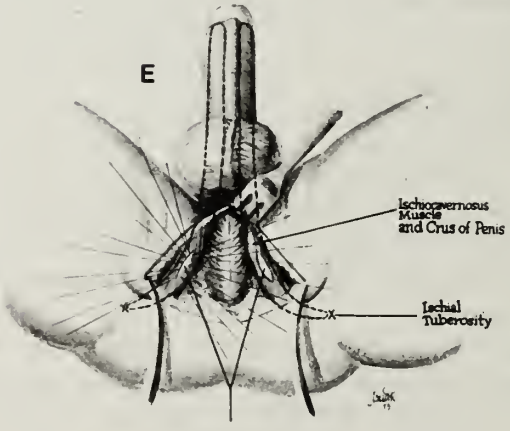


Figura 6

cavernoso, se puede dilatar hasta un número 10 o 11. Cuando se dilate debe tomarse gran cuidado de no perforar el crus. Al tiempo de la operación, todos los tamaños deben estar listos y disponibles. Nosotros

hemos encontrado que el tamaño 15.8 cm. (mediano) o el 17.0 cm. (largo) y el diámetro más ancho, son los generalmente requeridos. La prótesis debe encajar firmemente contra la pared del cuerpo cavernoso. El extremo distal de la prótesis debe extenderse hasta la punta extrema del cuerpo cavernoso para que el glande encaje de manera firma y correcta sobre la prótesis. Después de que una de las prótesis ha sido insertada, el mismo procedimiento es llevado a cabo en el otro lado (Figura 6). Las incisiones en cada cuerpo cavernoso son cerradas con suturas corridas 3-0 catgut crómico. El resto de la herida es cerrada de manera rutinaria. No se usan drenajes y el cateter uretral es removido inmediatamente que se finaliza la operación. Al inicio del procedimiento quirúrgico los implantes son puestos en remojo en una solución antibiótica y después de la implantación la herida es irrigada con la misma solución *. Además, todos los pacientes son tratados con un antibiótico de amplio espectro con anterioridad a la operación y se continuará con el mismo tratamiento por varios días después de la operación. El paciente se podrá dar de alta del hospital en cuatro o cinco días y coito es permitido en dos o tres semanas.

En aquellos pacientes que han quedado impotentes después de fractura de la pelvis y que se les ha hecho una uretroplastía, las incisiones pueden hacerse laterales, directamente sobre la crura, o ventralmente en la línea media de la unión penoescrotal para de esa manera evadir el área de cicatrices. El resto de la operación es idéntica a la descrita anteriormente.

La prótesis de pene Small-Carrión ha sido implantada a ciento diez pacientes desde febrero de 1973 hasta marzo de 1975 (Tabla I). Sus edades varían desde 19 hasta 72 años. Cuatro de los pacientes se encontraban impotentes después de una prostatectomía; dos de ellos después de priapismo; dos tenían impotencia psicogénica; once pacientes tenían impotencia causada por arteriosclerosis generalizada; tres estaban impotentes después de haberse fracturado la pelvis; quince de los pacientes tenían lesiones sufridas en la médula espinal; tres, tenían impotencia secundaria a diabetes y otro tenía epispadia y extrofia de la vejiga. Varios de los pacientes habían tenido con anterioridad prótesis Pearman, la que les resultó insatisfactoria debido a que les producía gran irritación en el glande y además no satisfacían a la mujer.

Las complicaciones han sido mínimas (Tabla II). Dos de los pacientes desarrollaron retención urinaria requiriendo cateterización por veinticuatro horas. Dos pacientes expulsaron la prótesis transuretralmente: uno de éstos había tenido insertado un catater uretral por un período largo de tiempo, además de haber sido previamente sometido a una prostatectomía transuretral y esfinterectomía. El paciente que expulsó la prótesis transuretralmente requirió cirugía en la unión penoescrotal y subsiguientemente desarrolló infección en la herida de uno de los cuerpos cavernosos. Después de la expulsión de la prótesis, las heridas y la uretra sanaron satisfactoriamente y ambos pacientes sostienen coito con la prótesis intracorporal restante aún cuando probablemente los resultados no son óptimos, En uno de los pacientes la colocación de la prótesis fue incorrecta y fue necesario removerla. Este fue un paciente que tenía un extenso tejido cicatrizal en el periné secundario a un absceso periuretral y uretroplastía proximal. Otros tres pacientes desarrollaron infecciones superficiales en las heridas, las cuales sanaron sin ninguna consecuencia.

El manejo adecuado de la impotencia siempre ha sido un enigma, tanto para los urólogos como para los otros médicos.

Antes de considerarse la implantación de esta prótesis, el paciente debe someterse a una evaluación urológica y endocrinológica. También debe habérsele tratado con un curso de andrógenos, aconsejado sexualmente, y haber recibido psicoterapia, sin beneficio alguno. Fisiológicamente, la colocación intracorporal bilateral tiene un gran sentido, porque es la que más se asemeja a una erección normal. En el lugar descrito anteriormente, la prótesis ofrece aumento en longitud, excelente soporte debido a la firmeza del cuerpo cavernoso en el ancho del pene. La prótesis Small-Carrión contiene todas estas ventajas. La forma y consistencia de una erección normal es obtenida usando una cubierta de silicona médicamente graduada con interior de esponja silicona. Esta prótesis es firme; sin embargo, tiene suficiente flexibilidad de modo que permite mantener el pene inconspicuo bajo el calzoncillo tipo atlético o bikine, bien en posición normal o sobre la pared abdominal. Para evitar cicatriz en el cuerpo del pene, se recomienda acceso quirúrgico perineal; no obstante, en pacientes con marcado endurecimiento periuretral o tejido cicatrizal, incisiones laterales o una incisión media más distante, puede ser

* - *Polymyxin-Neomycin. Burroughs Wellcome*

TABLA I
CLASIFICACION Y RESULTADOS DE PACIENTES CON PROTESIS SMALL-CARRION

Diagnóstico	Número de Pacientes	Resultados
Cystectomia, Posprostatectomía, Resección Abdominal Perineal	13	Excelente
Después de Priapismo	4	Excelente
Psicogénico	10	Excelente
Fractura de la Pelvis	6	5 Excelentes 1 Fracaso Parcial (Pérdida de la Prótesis secundaria a infecciôn)
Arteriosclerosis	30	Excelente
Daño en la Médula Espinal	15	13 Excelente 1 Fracaso Parcial (Pérdida de 1 Prótesis secundaria a infecciôn) 1 Fracaso (Colocación incorrecta de la Prótesis)
Diabetes Mellitus	24	Excelente 23-1 Fracaso-Infección
Epispadias y Extrofia de la Vejiga	1	Bueno (Pene Pequeño)

TABLA II

	Complicaciones	Número de Pacientes
1.	Retención Urinaria (temporera)	2
2.	Infección Severa de la Herida con Expulsión de la Prótesis	2
3.	Colocación Incorrecta de la Prótesis	1
4.	Infección de la Herida Superficial (sin consecuencias)	3
	TOTAL DE PACIENTES	110

utilizada para evitar disección a través de un perineo lleno de tejido cicatrizal. Los pacientes con incisión perineal pueden reanudar sus relaciones sexuales antes que aquéllos con incisión en el pene.

La inserción de esta prótesis en pacientes impotentes con daño en la médula espinal y vejiga neurogénica tiene una ventaja adicional, ya que con el aumento en longitud y periferia suministrado por la prótesis, permite a aquellos pacientes con un pene pequeño, los cuales tienen dificultad para mantener en su lugar un dispositivo externo para colección de la orina, lograrlo fácilmente de esa forma.

Se debe tomar precaución en los pacientes con vejiga neurogénica en quienes la descompensación de la vejiga está al límite. Prolongando y posiblemente comprimiendo el cuerpo de la uretra puede aumentar una resistencia capaz de producir más descompensación. Con la prótesis en su lugar, este caso puede

necesitar una esfinterectomía externa. Es aconsejable una completa evaluación de estos pacientes con anterioridad a la inserción de la prótesis y hacer cualquier cirugía transuretral que se requiera antes de la implantación. Si la prótesis ha sido implantada y más tarde se hace necesario una operación transuretral, el acceso a través de una uretrostomía perineal debe tenerse en cuenta.

Los anteriores descubrimientos en pacientes con vejigas neurogénicas y descompensación límite, han indicado una ventaja más en la prótesis Small-Carrión. En pacientes impotentes y parcialmente incontinentes después de una prostatectomía, extendiendo y comprimiendo la uretra, aumenta la resistencia para orinar y como resultado a cierto grupo selecto de pacientes incontinentes les ha dado control urinario.

En conclusión, los resultados con el uso de la prótesis Small-Carrión han sido excelentes en treinta y siete pacientes, y satisfactorio en uno de ellos. De los tres pacientes con complicaciones iniciales serias, en dos de ellos se obtuvo un resultado funcional adecuado. Las distintas ventajas y las posibles complicaciones con el uso de esta prótesis, al igual que la técnica quirúrgica Small-Carrión, han sido discutidas. Basándose en el material aquí presentado, estamos convencidos que esta prótesis ofrece una alternativa nueva y mejor a los tratamientos convencionales para la impotencia.

ARTICULOS A PUBLICARSE EN EL MES DE MAYO 1976

1. **Analysis of Electrocardiographic Abnormalities other than "Ischemic" S-T Depression Occurring During Submaximal Treadmill Exercise Testing** — *Esteban Linares Rivera, MD, Elí A. Ramírez, MD, FAPC, José A. Pereyó, MD.*
2. **Indications for His Bundle Recordings in the Clinical Practice of Cardiology** — *Juan M. Aranda, MD, Benjamín Befeler, MD and Agustín Castellanos, Jr., MD.*
3. **Manejo del Coma Hepático** — *Eduardo A. Santiago Delpín, MD.*
4. **Medicine and the Crisis - In Confidence** — *Edward H. Reinhard, MD.*
5. **Cardiovascular and Physiological Aspects of Sex** — *Charles D. Johnson, MD.*
6. **Síndrome Estiloideo: Presentación de Casos** — *Raúl Bertrán Escanoverino, MD.*

FORO DE MEDICINA NUCLEAR: PULMONARY EMBOLISM

Frieda Silva de Roldán, MD
Raquel Martínez, MD

A 45-year old white male was admitted in March 1975 to the Caguas Regional Hospital because of sudden onset of diaphoresis and dizzyness. He also had dyspnea on exertion and general weakness during the previous five months. A few days after the admission he developed swelling of his left leg. Anemia and albuminuria were found. Three weeks after his admission, while doing minimal physical effort, he developed acute pulmonary edema, which was relieved after appropriate treatment.

He was transferred to the Veterans Administration Hospital for further evaluation and management. Several days after being at the VA Hospital the patient developed left pleuritic chest pain and cyanosis. At this moment he was found with severe respiratory distress, wheezing in the left hemithorax and fine rales in the right chest. He also had tachycardia, S_3 and S_4 gallop and edema of the lower extremities. Arterial blood showed pO_2 = 68.2 mmHg, pCO_2 = 15.8 mmHg, pH = 7.5, HCO_3 = 12.8 and BE = 5.1. Perfusion (^{99m}Tc albumin macroaggregates) and ventilation (^{133}Xe) scans were performed (Figs. 1 and 2).

Pulmonary embolism and nephrotic syndrome secondary to renal vein thrombosis were diagnosed. Treatment with heparin was started.

Discussion

Pulmonary thromboembolism is an important cause of mortality and morbidity in many diseases. The diagnosis of this condition is difficult because of the great variety of signs and symptoms with which it may present. Available data suggests that antemortem diagnosis is established in only 30 percent of cases. At autopsy, with special techniques, the incidence of embolism exceeds 60 percent (1).

There is increasing awareness of the many conditions which lead to pulmonic thromboembolism. Renal vein thrombosis, although rare, has been frequently associated with this condition.

In the majority of patients the diagnosis of embolism remains difficult. Routine laboratory studies contribute little to the diagnosis. Chest X-ray findings can be non-specific and a negative x-ray does not exclude the diagnosis.

By introducing gamma emitting radionuclides attached to albumin macroaggregates or microspheres into the pulmonary vascular bed the distribution of arterial blood flow can be assessed. Thus if alterations in the normal pattern occur, they can be detected promptly.

The radioisotopic study must always be evaluated with the chest x-ray, to exclude non embolic causes of abnormalities in the perfusion. A negative study is of particular value when accompanied by a negative roentgenogram, for it then virtually eliminates the possibility of pulmonary embolism.

Several scintigraphic patterns have been described

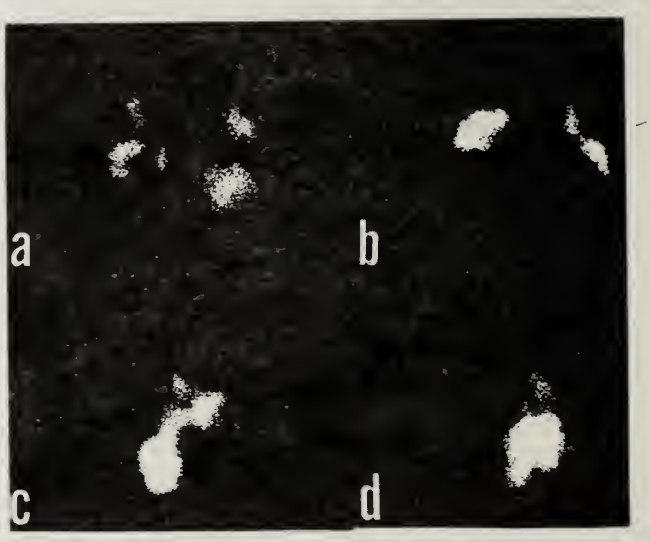


Figure 1: *Pulmonary perfusion study on March 19, 1975 (^{99m} Tc albumin macroaggregates) shows segmental regions of decreased perfusion on both lungs. (a) anterior, (b) posterior, (c) right lateral, and (d) left lateral views.*

From the Nuclear Medicine and Medical Services, Veterans Administration Hospital, San Juan, Puerto Rico.

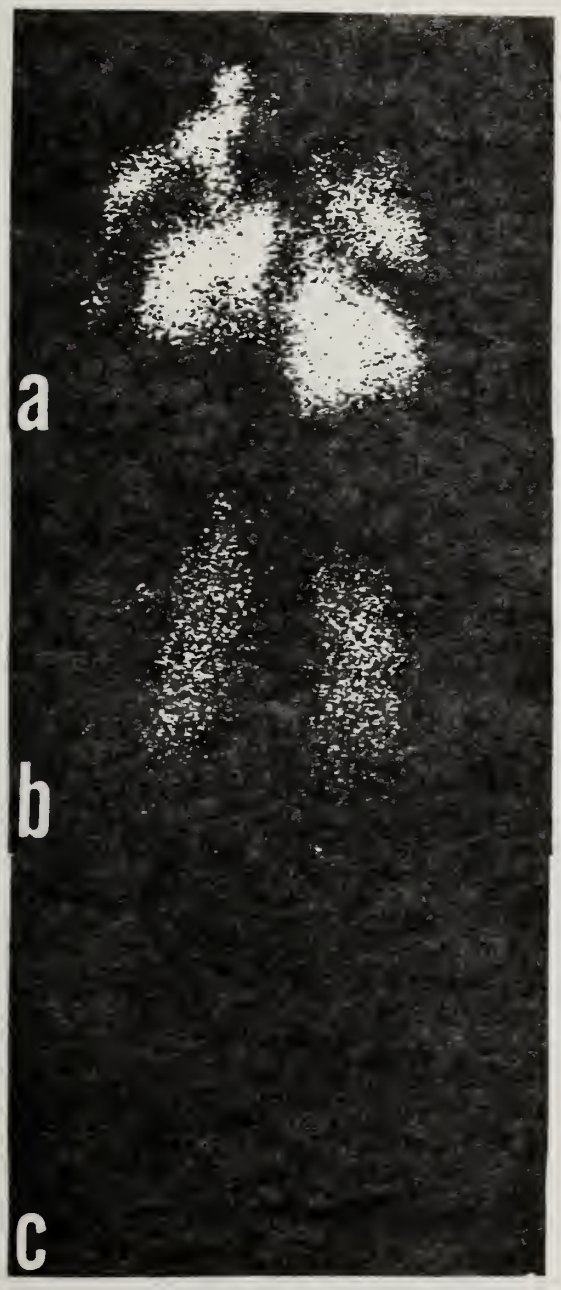


Figure 2: *Xenon ventilation-perfusion study on April 10, 1975 shows on the perfusion phase multiple defects on both lung corresponding to lung segments (a). On the ventilation phase (b), the previously mentioned segmental defects, filled with gas in an almost uniform way. In the washout phase (c) there is some delay in the passage of the material from the right lung as compared to the left.*

in association with the condition, which are illustrated in this case (2). Characteristically, a localized area of decreased radioactivity in an area supplied by a segmental or lobar artery, is adscribed to embolism. The "fissure sign" and circumferential hypoperfusion have also been associated with multiple small emboli (3).

Serial scanning provides an objective method for the determination of the course of the process. Scintigrams done at a three week interval provided an adequate follow up of the pulmonary perfusion in our patient. The vast majority of emboli resolve in the first ten to fourteen days, but this is variable and depends mainly on the nature of the emboli, patient's age and associated diseases, particularly congestive heart failure.

Radioactive gases have been used for the assessment of regional ventilation, perfusion and lung volumes. ^{133}Xe has been the most widely used isotope and may be administered either by inhalation or intravenous injection (4). This technique provides useful visual and numerical data of the perfusion and ventilation of the lung zones in only one view, but is important in the differential diagnosis of embolic and non-embolic conditions.

The complete Xenon study consists of three different parts. The perfusion phase permits evaluation of the distribution of pulmonary blood flow. The ventilatory phase allows the assessment of regional gas distribution and the integrity of the capillary alveolar transfer system. The washout phase measures the patency of the airways.

Two major patterns have been described associated with pulmonary vascular and non-vascular disease (5). The one here illustrated is a typical case of a pulmonary vascular problem. There are non perfused areas with normal or near normal ventilation. This pattern is characteristically seen in pulmonary embolism. Non vascular disease typically presents near normal perfusion with an irregular pattern on the ventilation.

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FROM THE NATIONAL FOUNDATION ON THE ARTS AND THE HUMANITIES, WASHINGTON, D. C. 20506

FOUR HUMANITIES SEMINARS FOR MEDICAL PRACTITIONERS TO BE SUPPORTED IN 1976 BY THE NATIONAL ENDOWMENT FOR THE HUMANITIES

The National Endowment for the Humanities will again support a program of humanities seminars for physicians and other members of the health professions in 1976. The seminars will bring medical practitioners together with distinguished humanists from the fields of history, religion, sociology, and philosophy for a month of full-time study devoted to such issues as ethical conflicts, the rights of patients and practitioners, the purpose and limits of the medical professions and their relations to the community.

Up to 15 participants will attend each seminar tuition free and will receive a $1,200 stipend to cover expenses, plus reimbursement for travel up to a $300 maximum. Participants may be accompanied by members of their families, but the stipend will not be increased.

John C. Burnham, Professor of History and Lecturer in Psychiatry at The Ohio State University, will direct a seminar on his University's campus August 9-September 3. The aim of this seminar will be to identify the particular historical forces which have shaped the medical profession and determined the direction of its development. It will attempt to sharpen the participants' understanding of their profession by studying it in the context of Western culture and how it has been involved in the forces of social change.

H. Tristram Engelhardt, Jr., a philosopher and physician who is Associate Professor of the Philosophy of Medicine in the Institute for the Medical Humanities of the University of Texas Medical Branch at Galveston, will direct a seminar at his University September 13-October 8. The seminar will examine the general issue of patient's rights and the particular issue of the right to health care through a consideration of the basic philosophical and ethical issues that bear on the status of the individual, the nature of justice, and the relationship between the individual and society.

Renée C. Fox, Professor of Sociology in the Departments of Sociology, Psychiatry and Medicine at the University of Pennsylvania in Philadelphia, will conduct a seminar on her University's campus June 1-30. The seminar will examine from a cross-cultural perspective the ways in which social and cultural forces influence certain present-day medical phenomena and problems in American society. Conceptions of health and illness, the process of professional development, the hospital as a social system, modern medical research, and bio-ethical issues in contemporary medicine are among the topics to be considered.

William F. May, Professor and Chairman of the Department of Religious Studies at Indiana University in Bloomington, will direct the fourth seminar on the Stanford University Campus in Stanford, California June 28-July 23. Participants will explore basic ways of interpreting human nature and obligation as they affect decisions in medical practice. The seminar will also attempt to clarify the role of the practitioner in the several communities in which he or she operates, including the doctor-patient relationship, the family facing medical crisis, the decision-making ethos of the hospital, and the claims of society at large.

Applications are invited from physicians and other members of the health professions, including public health officials, nurses, hospital administrators, executives of professional societies, and others. Selection of participants will be made by the seminar directors with the advice of selection committes. The application deadline for the University of Pennsylvania and Stanford University seminars is April 15, with selections to be announced about April 22. The application deadline for The Ohio State University and University of Texas seminars is May 13; selections will be announced about May 28.

Further information, including a leaflet describing the seminars in greater detail and application forms, may be obtained from:

Professor John C. Burnham
Department of History
The Ohio State University
230 West 17th Avenue
Columbus, Ohio 43210

Professor Renée C. Fox, Chairman
Department of Sociology
128 McNeil Building CR
University of Pennsylvania
Philadelphia, Pennsylvania 19174

Professor William F. May, Chairman
Department of Religious Studies
Sycamore Hall 230
Indiana University
Bloomington, Indiana 47401

Professor M. Tristram Englehardt, Jr.
Institute for the Medical Humanities
University of Texas Medical Branch
Galveston, Texas 77550

HEW NEWS:

The Department of Health. Education. and Welfare today proposed regulations which would permit supplemental security income recipients to request termination of benefits if they qualify for other benefits which would be more advantageous to them.

Present regulations do not specify how a recipient can ask for voluntary termination of benefits, except by withdrawal of the initial claim, which would require him to repay all the money previously paid.

Another proposal change in present regulations would give the Social Security Administration the authority to deny or suspend eligibility for supplemental security income if the applicant or recipient refuses to furnish information or fails to comply with a request necessary to determine his initial or continuing eligibility for the program.

Interested parties have 30 days to submit comments after today's publication of the proposed regulations in the Federal Register.

The Department of Health, Education, and Welfare today proposed regulations increasing the dollar amounts people can earn and still be considered disabled for purposes of receiving social security and supplemental security income disability checks.

The proposed regulations raise the monthly earnings guidelines to be used by the Social Security Administration in 1976 to determine when work by a disabled beneficiary is considered "substantial gainful activity." Under the law, a person able to perform substantial gainful activity is not eligible to receive monthly disability benefits.

The proposed regulations, published in today's Federal Register, would:

– Increase from $200 to $230 monthly the earnings guide for determining when work is substantial gainful activity. When a person works for average monthly earnings greater than $230 he ordinarily would be considered able to engage in substantial gainful activity.

– Provide that if a person's earnings average between $150 and $230 per month, the nature of the person's work activities and the medical evidence relating to his condition will be considered in determining whether the individual is eligible for disability benefits. The current range is $130 to $200.

– Increase from $130 to $150 a month the amount of average monthly earnings that ordinarily will not be considered "substantial gainful activity."

The proposed regulations also provide for a systematic adjustment of these earnings guidelines on the basis of yearly changes in the average taxable earnings of all persons reported under the Nation's social security system.

These guides apply only to disabled claimants and beneficiaries under social security and supplemental security income. They do not apply to retired workers, survivors, or dependents. Earnings limitations for these beneficiaries are set by other provisions in the social security law.

Interested parties have 30 days after today's publication in the Federal Register to submit comments.

AMA NEWSLETTER:

A HOUSE SUBCOMMITTEE REPORT TITLED "UNNECESSARY SURGERY" is "unsound in concept" and "unscientific in method." the AMA told the subcommittee chairman this week. "The staff of the subcommittee have done you a great disservice," AMA Executive Vice President James H. Sammons. MD, said in a letter to Rep. John E. Moss (D-Calif.). The report of the Subcommittee on Oversight and Investigations also "contains errors in data and information, distorts testimony.... and bases its main conclusions on an incomplete and improperly defined study," Dr. Sammons said. "We must conclude that the report submitted to you by the staff is nothing more nor less than a dishonest piece of political propaganda." The report, issued late in January, said Americans spent $3.9 billion on 2,300,000 unnecessary operations that resulted in 11,900 deaths.

The Subcommittee Used 17 Percent as the rate of unnecessary surgical procedures, although the source for the figure, Eugene G. McCarthy, MD, of Cornell U, pointed out that it represents "not confirmed" procedures. Dr. McCarthy also told the subcommittee that his study was not a study of unnecessary surgery and that it included no follow-up on how many of the 17 percent needed the operation later on. Dr. Sammons wrote: "Despite the staff's knowledge that (the 17 percent figure) was not an accurate and final figure even by the staff's own applied definition, the staff used it as the basis for all its projections. Mr. Chairman, I leave it to your own judgment as to whether such methodology is honest or dishonest."

The AMA Letter to Moss cites the report's misrepresentation of savings possible by the elimination of so-called unnecessary surgery. Error is inherent in the grossly inflated figures reached by nationwide projection, although Dr. McCarthy in his study noted that "the findings presented here cannot be applied to the general population undergoing elective operations." Moreover, the AMA said, no allowance for the expense of alternative methods of care is made in the computations. "Yet the subcommittee, once again, was told by Dr. McCarthy that such costs—as well as the costs of second consultations (estimated at about $50 per case)—must be offset against any projected savings. No such offset was made. All the subcommittee staff did was multiply its estimated number of unnecessary surgeries by its own estimate of the cost of a surgical procedure ($1,650). This, again, is patently dishonest and results in an exaggerated figure."

Testimony Before the Subcommittee was distorted in the report, the AMA pointed out. The subcommittee said it used "six categories of unnecessary surgery" developed by George Zuidema, MD, of Johns Hopkins School of Medicine, but Dr. Zuidema had told the subcommittee that his study defined "certain categories of operations which would require cla-

rification before one could decide whether the procedure was necessary or unnecessary." Ignored in the report is Dr. Zuidema's comment that the allegations as to unnecessary surgery are "totally unsupported by data."

In Its Report the Subcommittee recommended that HEW require a second professional opinion for all Medicare-Medicaid surgery and that HEW undertake a study "to determine the differences in health indices, costs and surgical procedure rates between salaried surgeons and fee-for-service surgeons." Dr. Sammons said the AMA endorses "the idea of second consultation in high risk cases or when medically appropriate" and has "so recommended on numerous occasions." He noted that the report ignores testimony that second consultations and peer review programs have been developed by the private sector. The report's recommendation expresses no apparent interest in a consideration of those patients being denied necessary surgery under prepaid plans," he said.

We Reject the Notion that Americans have been subjected to millions of unnecessary operations, that have wasted billions of dollars, and cost thousands of lives," the AMA said. "Such allegations by the subcommittee staff are unsupported and unsupportable. We reject the slanderous and insulting notion that surgeons are primarily motivated by money and that prepaid group practice would eliminate all unnecessary surgery. Such a proposition is unproven, unprovable and flies in the face of testimony presented before the subcommittee."

ANNOUNCEMENT FROM THE DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, ROCKVILLE, MARYLAND, 20852

A nationwide network of area health planning agencies will be established by the Department of Health, Education, and Welfare by June 30 under a timetable published this month in Public Health Reports, an official Departmental magazine.

The agencies are part of the health planning structure established under the Health Planning and Resources Development Act of 1974, the provisions of which are described in an article by Eugene J. Rubel, Acting Director, Bureau of Health Resources Development, in HEW's Health Resources Administration.

Last September HEW formally divided the country into 202 health service areas, in accordance with the law, Rubel explains. Currently, a Health Systems Agency is being designated for each of those areas to conduct health planning and related functions.

Rubel said the agencies would be designated and funded by June 30, with membership coming from each of the areas served. State agencies would be responsible for drawing the area plans into State plans.

The January-February issue of Public Health Reports contains a special section of 11 articles on various aspects of the health planning law by governmental and nongovernmental health officials and experts.

The articles cover regulatory and review functions of agencies created by the new law, sources of health planning information, training of planning personnel, the role of health care consumers in health planning, and similar topics.

The magazine is the official journal of HEW's Public Health Service.

SE VENDE

Vendo casa de dos plantas localizada en Urb. Altamira, Calle Aldebarán 582. Frente Avenida Guaynabo, a pasos centros comerciales. Gem. San Patricio Plaza. Propia para consultorio médico o policlínica. Si es veterano sin pronto pago solo gastos de cierre. Favor llamar al 723-6780.

Instrucciones para los Autores

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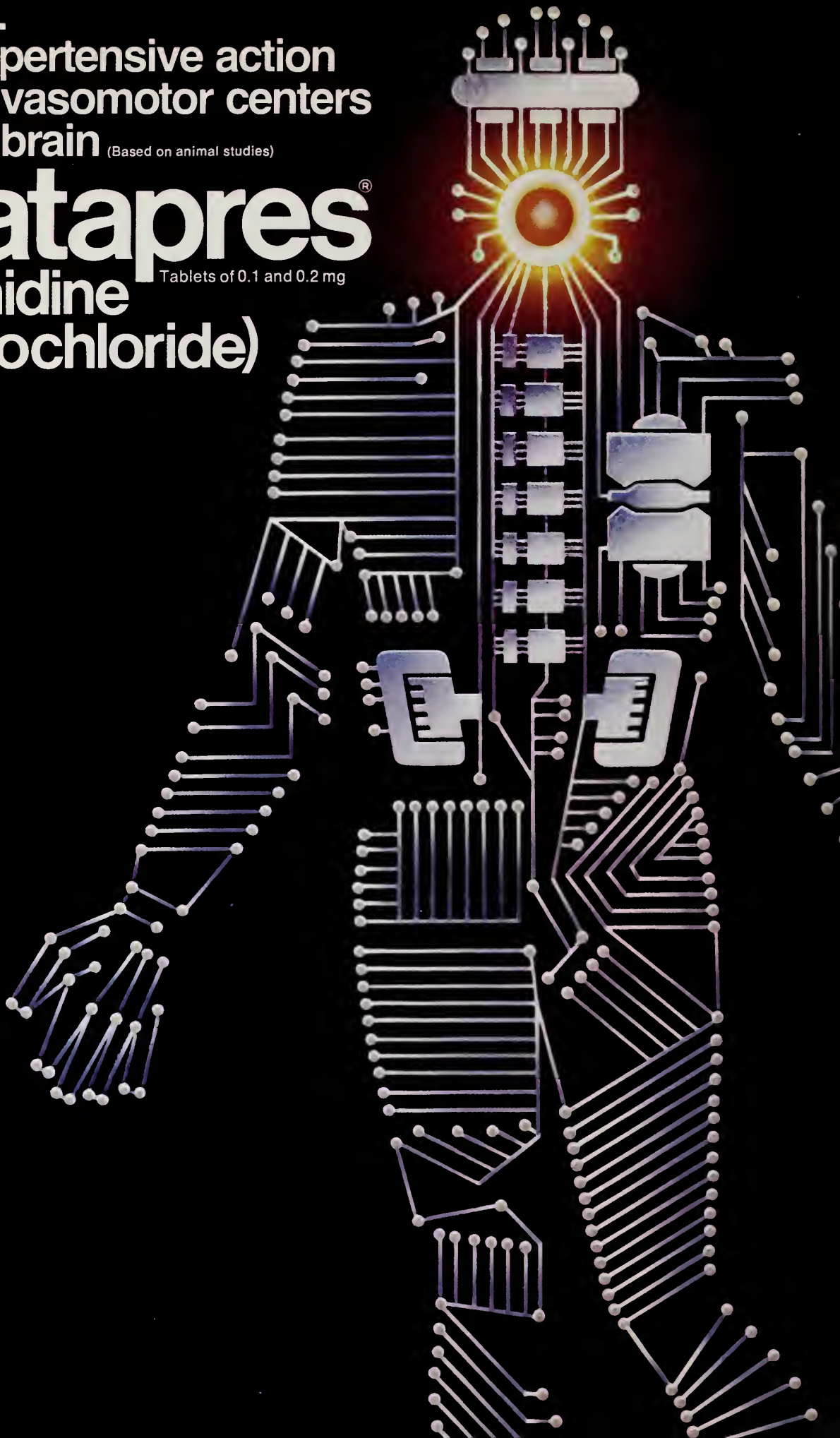
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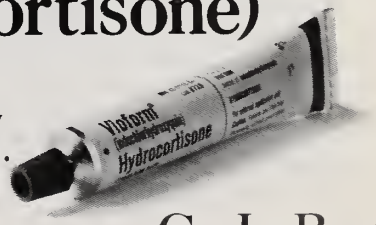
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ANALYSIS OF ELECTROCARDIOGRAPHIC ABNORMALITIES OTHER THAN "ISCHEMIC" S-T DEPRESSION OCCURRING DURING SUBMAXIMAL TREADMILL EXERCISE TESTING

Esteban Linares-Rivera, MD
Elí A. Ramírez, MD, FACP
José A. Pereyó, MD

The most significant criterion for the inadequacy of myocardial oxygen supply during exercise is the "ischemic" depression of the ST segment (1). This has been defined as ST segment depression which is initiated by J point depression of 0.1 mv or more followed by an ST segment which is flat or downsloping for a duration of 0.08 second or more. Other criteria reported as a positive response to exercise testing are dysrhythmias (bursts of ectopic beats, ventricular tachycardia, ventricular fibrillation), transient bundle branch block (either righr or left), atrioventricular conduction defects and negative U waves (2, 3, 4). There is no general agreement about the significance of these abnormalities, but it is accepted that they are less reliable in predicting ischemic heart disease than the "ischemic" ST depression.

We have analyzed different abnormalities observed in our patients during exercise testing correlating them with the classical "ischemic" ST depression, the result of coronary arteriography and both.

Materials and Method

Treadmill submaximal exercise tests were done at the Exercise Laboratory of the San Juan Veterans Administration Hospital, following the general guidelines described by Sheffield *et al* (5). The electrocardiographic exercise test heart rate tables of Lester *et al* (6, 7) and the Multistage Exercise Capacity Test table of Doan *et al* (8) were used. The starting stage of exercise was selected according to the clinical features of the subject being tested. Patients with severe symptoms were started at the lowest level (Stage I) while others were started at Stage II which is a near equivalent to the double step test of Master. Each exercise stage was continued for five minutes. A bipolar V_5 chest lead was monitored continuously throughout the test and the peak maximum heart rate was calculated starting 30 seconds before the stage was concluded. Recordings were made prior to exercise in the recumbent and standing positions, during exercise, and after exercise, every two minutes for at least six minutes. If the test was ne-

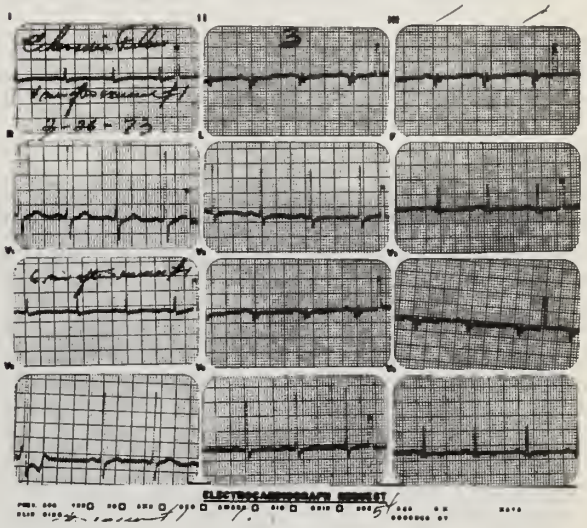


Fig. 1: *Post extrasystolic T wave inversion is noted in V_4 after a PVC. Leads taken after exercise were: I, II, AVF, V_4, V_5 and V_6.*

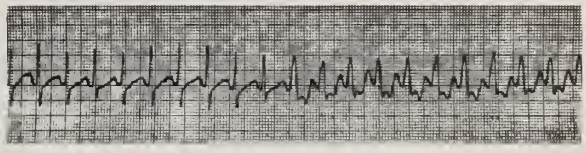
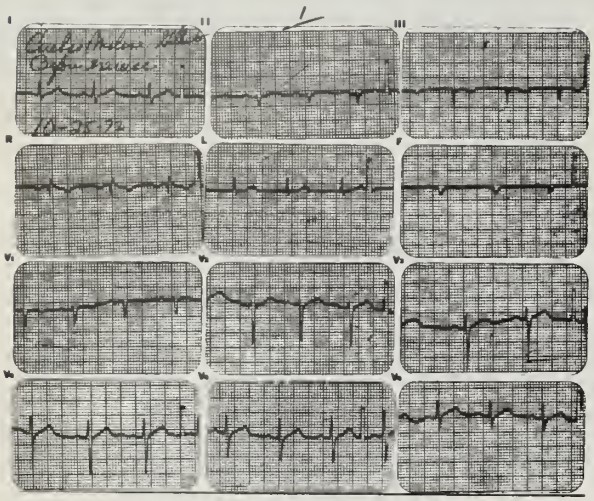


Fig. 2: *Modified V_5 monitored lead showing rate dependent LBBB at a rate of 158/min. This was the third GXT on this patient and the previous ones showed the same phenomena at a heart rate of 158/min.*

From the Cardiology Section, Medical Service, Veterans Administration Hospital, San Juan, P. R.

Presented in part at the Puerto Rico Heart Association Annual Meeting, Sept. 22, 1973.



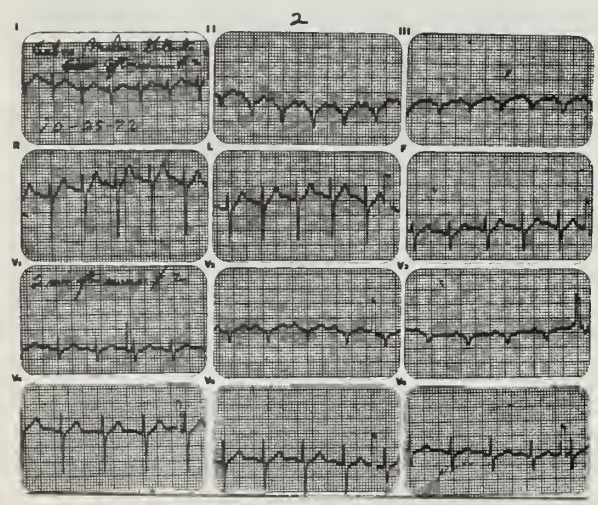


Fig. 3: *Before exercise QRS duration in lead 2 is .06 seconds. After exercise it increases to .08 seconds.*

gative, the next higher stage of exercise was then started. Exercise was progressively increased until either the patient developed symptoms severe enough to stop the test, or achieved 80 percent of expected maximum heart rate for age, or developed "ischemic" ST changes. Tracings were subsequently recorded every two minutes for ten minutes until ST changes, if present, had disappeared. All tests were performed on patients referred because of anterior chest pain who were clinically stable and ambulatory. All tests were conducted under the direct supervision of a physician and complete resuscitation facilities were constantly available.

Criteria for a positive exercise test were the "ischemic" ST

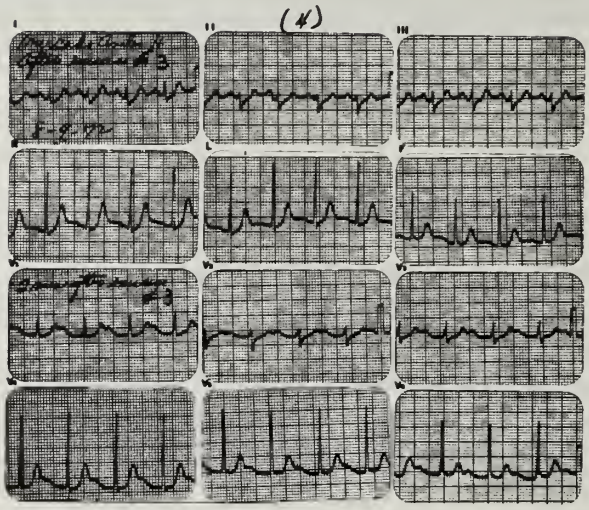


Fig. 4: *Immediately after exercise, PR interval measures .16 seconds (lead 2, upper strip). 2 minutes after exercise, PR interval is prolonged to .31 seconds.*

depression described above in all except two patients: one who developed ventricular tachycardia and another who developed transient left bundle branch block during exercise.

Results

Premature Ventricular Contractions

During a 16 months period 146 patients had 156 treadmill submaximal exercise tests. Their ages ranged from 20 to 66 years and there were 143 men and 3 women. Forty six patients who had both graded exercise test (GXT) and coronary arteriography are the subject of this report.

Eight patients showed at least one premature ventricular contraction (PVC) after exercise (see Table I). This represents an incidence of 17.4 percent of this group. Six of the eight patients with PVCs after exercise had significant coronary artery disease (75 percent). Specifically there were 4 with double vessel disease and 2 with triple vessel disease (they were the only 2 patients with triple vessel disease in the whole group). Two patients had normal coronaries or insignificant coronary disease.

TABLE I
INCIDENCE OF PVC'S AFTER GXT IN 46 PATIENTS WHO ALSO HAD CORONARY ARTERIOGRAPHY DONE *

	No. of Patients	Patient's with PVC'S after Ex.	Coronary +	Arteriography −
Ex. Text +	14	4 (28.6 percent)	4	−
Ex. Test −	32	4 (12.5 percent)	2	2
Totals	46	8 (17.4 percent)	6 (75 percent)	2

** - Positive coronary arteriogram was considered when 50 percent obstruction of at least one major coronary vessel was present.*

TABLE II

		LEFT VENTRICULAR MOTION DISORDER		
		YES	NO	TOTAL
PVC'S	YES	7	1	8
	NO	20	15	35
				43

Four patients with PVCs after exercise and positive GXT showed significant coronary artery disease; 2 patients with two vessel disease and 2 with triple vessel disease.

In contrast, of the 4 patients with PVCs after exercise, but negative GXT, 2 patients had normal coronary arteriograms and 2 had two vessel disease. This suggests that the presence of PVCs in combination with a positive GXT may add to the probability of significant coronary artery disease. However, the number of cases is too small to reach a definite conclusion.

Of the group of 38 patients who did not show PVCs after exercise, there were 3 who had single vessel disease and 6 who had double vessel disease, for a total of 9 patients with significant coronary artery disease in this group of patients (24 percent).

Forty three patients had left ventriculography and GXT. Seven of 8 patients with PVCs after exercise showed left ventricular motion disorder either loca-

Post-extrasystolic T wave inversion

There was only one patient in this series who exhibited this phenomenon. He was a 54 year old male patient who had clinical electrocardiographic evidence of an old diaphragmatic myocardial infarction. One and a quarter minutes after starting treadmill exercise in Stage I, he developed angina and the procedure was stopped. He achieved only 70 percent of his expected maximum heart rate adjusted for age and no ST displacement was observed. Coronary arteriogram revealed two vessel disease. Left ventriculography showed moderately decreased contractility of the left ventricle. Left ventricular end diastolic pressure was 18 mm. Hg and cardiac output was normal.

Intermittent Left Bundle Branch Block

This was also observed in one patient. He was a 49

years old male with clinical and electrocardiographic evidence of an old anteroseptal myocardial infarction and probable old diaphragmatic infarction. He had mild hypertension, type I hyperlipoproteinemia and diabetes mellitus controlled with diet alone. Three and one half minutes after the beginning of treadmill exercise at Stage II he developed left bundle branch block. The procedure was stopped and four minutes later the left bundle branch block disappeared. No ST changes were observed afterwards. Coronary arteriogram revealed single vessel disease: specifically 75 percent proximal obstruction of the left anterior descending coronary artery. Right and left heart hemodynamics as well as left ventriculogram were essentially normal.

Intraventricular Conduction Defect

A 43 year old male patient with clinical electrocardiographic and vectorcardiographic evidence of an old diaphragmatic myocardial infarction developed after exercise a transient increase in QRS duration from .06 second to .08 second. He was found to have a normal coronary arteriogram as well as normal right and left heart hemodynamics and left ventriculogram.

First Degree A-V Block

A 48 year old male patient with mitral insufficiency due to rheumatic heart disease developed on two different occasions a first degree AV block after exercise. His coronary arteriogram was normal.

Discussion

A recent study by Goldschlager *et al* (9) suggests that exercise-precipitated PVCs may represent a form of subclinical ischemia and may serve as an aid in detecting potentially high risk patients. Our findings are in agreement with this impression. In addition, they suggest that the combination of PVCs and positive GXT correlates better with significant coronary artery disease than either alone. However, additional data is needed to support this suggestion.

According to Scherf (10) the inversion of an otherwise normal T wave in the first post-extrasystolic beat tends to indicate structural heart disease. However, different types of heart diseases have been associated with this finding indicating that the pathogenesis may not be specific for any one etiologic process. Furthermore, Edmands and Bailey (11) have shown that the post-extrasystolic T wave change is basically a normal phenomenon which correlates with the magnitude of the post-extrasystolic contractile change. The observed association of the post-extrasystolic T wave change with myocardial disease may reflect the relatively greater post-extrasystolic contractile change associated with increased duration of the contractile state. This mechanism may be possible in our case since he had a moderately decreased contraction of the left ventricle as seen in the left ventriculogram.

Ischemic and hypertensive heart disease or a combination of both have been found to be the underlining etiological factors in most of the reported cases of intermittent left bundle branch block. This condition has also been associated in rare instances with syphilitic heart disease, rheumatic heart disease, thyrotoxicosis, anemia, diphteria, sepsis and a number of drugs with depressant effect on cardiac conduction such as quinidine, procainamide, and potassium (12).

Carter (13) postulated that in patients with incomplete bundle branch block a few intact fibers of the conducting bundle were carrying on the normal excitation process under favorable conditions, and a minor local circulatory insufficiency might be responsible for failure of the surviving fibers to conduct. This theory was confirmed by Baschmakoff (14). He also showed that if a strip of conducting tissue was narrowed, the conduction was normal at a slow rate but became impaired at rapid rates. As in our case, rate dependency has been demonstrated in most of the patients with left bundle branch block (15). However, this may not have been the only mechanism in our patient. The left main bundle has a dual blood supply from the anterior descending and from the right coronary arteries. As our patient had significant disease of the left anterior descending coronary artery, it is possible that during exercise he developed left bundle branch block because of functional block of the main left bundle produced by ischemia.

The significance of the isolated intraventricular conduction defect manifested by prolongation of the QRS after exercise in our one patient remains undetermined.

The presence of a prolonged PR interval (greater than 20 second) has been associated with a high incidence of associated coronary heart disease (16). Other causes are congenital heart disease, chronic rheumatic heart disease, digitalis intoxication as well as other miscellaneous causes. In our patient the first degree A-V block was proven by His bundle studies to be due to block above the His bundle (supra-His block).

Summary

The relationship between electrocardiographic abnormalities observed during graded exercise test (GXT) and coronary arteriography in 46 patients are discussed.

We suspect that the findings of both PVCs and significant ST changes during GXT correlated better with significant coronary artery disease than either one alone. However, we still need additional data to substantiate this finding.

Other abnormalities briefly discussed were: Post-extrasystolic T wave inversion; intermittent LBBB; intraventricular conduction defect and first degree AV block.

Resumen

Se discuten las relaciones entre varias anormalidades misceláneas electrocardiográficas observadas después de ejercicio con los hallazgos clásicos "isquémicos" de depresión del segmento ST, y con los hallazgos arteriográficos en 46 pacientes. Sospechamos que la combinación de contracciones prematuras ventriculares con cambios significativos de ST durante la prueba graduada de ejercicio pueda tener mejor correlación con la presencia de lesiones significativas en las arterias coronarias que cada uno de estos hallazgos por separado. Sin embargo, se necesitan datas adicionales para verificar esta sospecha.

Se discuten brevemente otras anormalidades observadas durante la prueba de ejercicio a la luz de presentes conceptos. Estas incluyen inversión post-extrasistólica de la onda T, bloqueo intermitente de rama izquierda, defecto de conducción intraventricular, y bloqueo atrioventricular de primer grado.

Acknowledgment

We wish to express our appreciation for the assistance and help provided by Mr. José Arrache.

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INDICATIONS FOR HIS BUNDLE RECORDINGS IN THE CLINICAL PRACTICE OF CARDIOLOGY

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His bundle electrocardiography (HBE) combined with electrical stimulation of the heart has provided a sophisticated means of evaluating the conduction system of the heart (1-2). His bundle recordings have enhanced our understanding of arrythmias (3), the Wolff-Parkinson-White syndrome (4-5) and the site of conduction abnormality in patients with various forms of heart block (6). In addition the technique has been utilized extensively to study different physiologic (7) and pharmacologic interventions in experimental animals (8-9). On the other hand, it has been stated that the usefulness of HBE in the management of patients with heart disease has been limited and that its role in the routine care of cardiac patients is yet to be determined (10).

The clinical data and follow up of the last 30 patients who had undergone HBE in our institution were reviewed with special emphasis on the contribution of this technique in the management of the patients. The following cases illustrate the potential value of His bundle electrograms in the evaluation of patients with conduction disturbances.

Methods

The technique for His bundle recordings used in our department has been previously described (11). A tripolar catheter is introduced percutaneously through a femoral vein and is positioned across the septal leaflet of the tricuspid valve. Two bipolar leads with interelectrode distances of 1 and 11 mm respectively (HBE_1 and HBE_2) leads are recorded. In addition, two bipolar catheters with interelectrode distance of 1 mm and 1 cm are introduced through an intecubital vein and placed in the high right atrium for recording (1 mm) and pacing (1 cm). The terminals from the electrodes are fed into a distribution switch box, the outputs of which are connected to the input of the recording instrument (Electronics for Medicine, White Plains, New York). Leads 1, 2, AVF and V_1 are obtained simultaneously with the filtered (400-2000H_2) bipolar or unipolar intracardiac leads. The stimulator used for continuous coupled or paired pacing delivered slightly underdamped pulses, 2.5 msec in duration and twice the diastolic threshold values (12). During atrial paired pacing the interval between the driving (St_1) and testing stimuli (St_2) is progressively shortened in order that the whole cycle might be scanned. His bundle pacing was performed in two of the patients reported (Cases 1 and 3). The following intervals were measured during sinus rhythm and continous atrial pacing:

1. P-A interval (representing intra-atrial conduction time) was measured from the beginning of the P wave in the surface leads to the local atrial electrogram in the HBE leads (normal values 20-40 msec).
2. A-H interval (A-V nodal conduction time) was measured from the onset of the local atrial electrogram in the HBE lead (low right atrium) to the initial deflection of the His electrogram (normal value 50-120 msec) (11).
3. H-V interval (conduction time in specialized ventricular - Purkinje system) was measured from the initial deflection of the His electrogram to the onset of ventricular depolarization (QRS) in the surface or HBE leads (normal 35-55 msec).

Informed consent was obtained from each patient prior to the study.

Case Presentations:

Case 1: This 69 year old male was admitted to the hospital for evaluation of dizzy spells and one syncopal episode. An electrocardiogram taken in 1969 was normal except for left anterior hemiblock. A second tracing taken in 1973 (6 months before admission) showed complete LBBB with normal axis in the frontal plane. The PR interval was 0.18 seconds. The electrocardiogram at the time of admission showed complete LBBB with a QRS axis of -40 in the frontal plane (Figure 1). The PR interval was 0.20 seconds. The results of the physical examination were negative except for paradoxical splitting of the second heart sound. There was no evidence of postural

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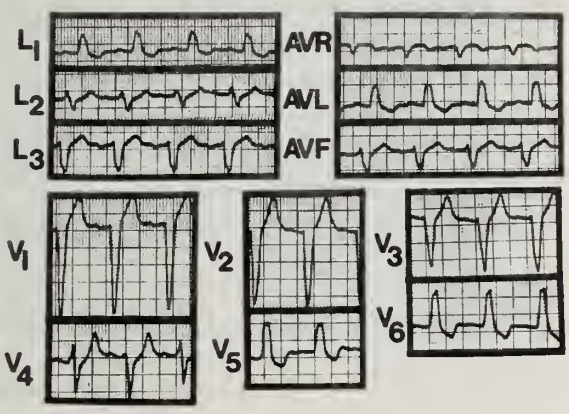


Fig. 1: *Case 1 - Electrocardiogram obtained at the time of admission. Complete left bundle branch block with left axis deviation is noted. The PR interval is 0.20 seconds.*

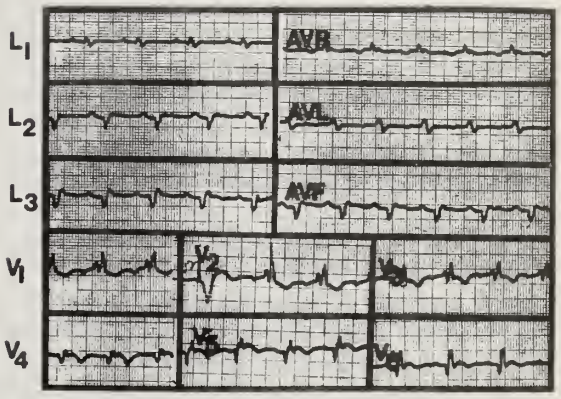


Fig. 3: *Case 2 - Electrocardiogram 48 hours after admission to the CCU. Complete RBBB, marked left axis deviation and prolonged P-R interval are noted. A paced beat is seen in* V_2.

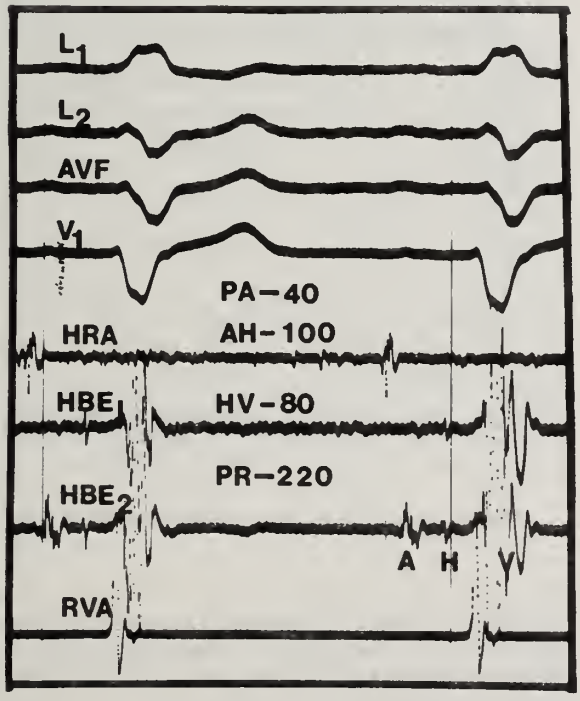


Fig. 2: *Case 1 - His bundle recordings revealed normal P-A and A-H intervals. The H-V interval was significantly prolonged to 80 msec. The PR interval was 220 msec, the rate 68 per minute.*

hypotension or hypoglycemia. The chest x-ray revealed the heart size to be in the upper normal limits. Skull series, brain scan as well as a complete neurological work up were negative. Several 24 hour Holter monitoring studies showed sinus tachycardia with occasional premature atrial contractions.

Electrophysiological Studies:

On the day of the procedure the resting sinus rate was 68 beats per minute (Figure 2). The PR interval was 220 msec. The P-A and A-H intervals were normal, however, the H-V interval was prolonged to 80 msec. During atrial pacing the patient developed block proximal to the His bundle (in the A-V node) at a pacing rate of 140/minute (normal response).

In view of the electrophysiologic findings and considering the clinical picture suggestive of episodic complete A-V block, a permanent demand ventricular pacemaker was recommended. After insertion of the cardiac pacemaker, the neurologic symptoms disappeared and the patient has been asymptomatic for 12 months. In his last clinical evaluation, inhibition of the permanent pacemaker with external chest wall stimulation revealed complete atrio-ventricular block with an escape ideoventricular rhythm at a rate of 45 per minute.

Comments:

The important therapeutic decision taken in this patient demanded a critical review of the significance of prolonged H-V intervals in patients with bundle branch block. In these cases, H-V prolongation reflects conduction delay in the functioning bundle branch and is a manifestation of bilateral bundle branch block (6, 13). Previous reports suggest that

patients with the electrocardiographic findings of bifascicular block (or partial bilateral bundle branch block) have an increased risk of developing complete atrioventricular block, which may result in transient neurologic symptoms (14-16). However, partial bilateral bundle branch block (bifascicular block) may be an incidental electrocardiographic finding and complete A-V block may never develop in patients with this pattern (17). His bundle electrocardiography allows localization and perhaps quantification of A-V conduction disturbances. Narula and Samet (18) reported marked prolongation of the H-V interval (mean of 85 msec) in patients with RBBB and left anterior hemiblcok who subsequently developed higher degrees of A-V block. Our observations agree with the data presented by Scheinman et al (19) who suggested that patients with transient neurologic symptoms, bifascicular or LBBB associated with marked prolongation of the H-V interval (> 80 msec), should be seriously considered as candidates for insertion of permanent cardiac pacemakers even in the absence of documented high grade or complete A-V block.

Case 2: A 49 year old male, with a previous myocardial infarction in 1971, was admitted to the CCU because of severe retrosternal chest pain and diaphoresis of 2 hours duration. The electrocardiogram showed an old infero-posterior myocardial infarction, narrow QRS complex, marked left axis deviation and elevation of the ST segment in the anterior precordial leads. Forty-eight hours after admission, he developed complete RBBB and a PR interval of 0.23 sec (Figure 3). His bundle electrograms recorded at the time of insertion of a temporary prophylactic pacemaker revealed a prolonged H-V interval of 60 msec. Fourteen days after admission the electrocardiogram (Figure 4) showed sinus rhythm with a prolonged PR interval, marked left axis deviation suggestive of left anterior hemiblock and a recent antero-lateral myocardial infarction. The RBBB reverted to an intraventricular conduction disturbances with a QRS complex of 0.10 to 0.11 sec.

Electrophysiologic Studies:

His bundle electrograms (Figure 5) showed normal P-A and H-V intervals. The A-H interval (A-V nodal conduction time) was prolonged to 130 mseconds. Atrial pacing up to a rate of 110 per minute showed prolongation of the A-H interval to 145 msec. No evidence of block proximal or distal to the His deflection was observed. The patient was discharged home without a permanent pacemaker, but he moved to another city three months later.

Comments:

The mortality rate associated with incomplete bilateral bundle branch block complicating acute myocardial infarction is high (20, 21). The primary cause of death has been thought to be cardiogenic shock or arrhythmias including complete heart block, systolic and ventricular fibrillation (21-22). Although the insertion of a temporary prophylactic pacemaker is still controversial, many authors recommend insertion but are aware that the benefit will be small (16, 20, 23-25).

Recent reports have suggested that His bundle recordings may be of clinical importance in patients with acute myocardial infarction complicated by incomplete bilateral bundle branch block (26). These observations suggest that those patients with bifascicular block and prolonged H-V intervals are at a higher risk for developing complete A-V block. His bundle

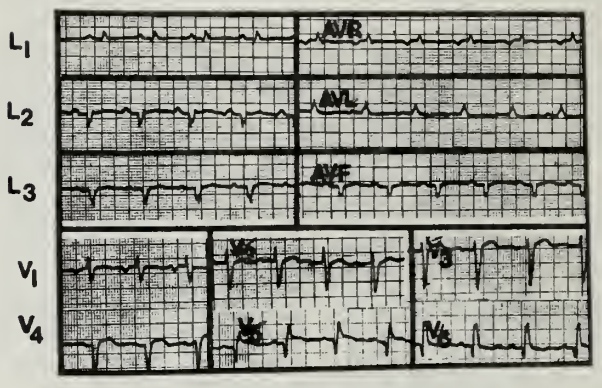


Fig. 4: *Case 2 - Electrocardiographic tracing recorded 14 days after admission to the CCU (12 days after insertion of temporary pacemaker). Note the prolonged PR interval, marked left axis deivation and an intraventricular conduction disturbance with a QRS complex of 0.10 to 0.11 seconds. An old infero-posterior as well as a recent antero-lateral myocardial infarction are present.*

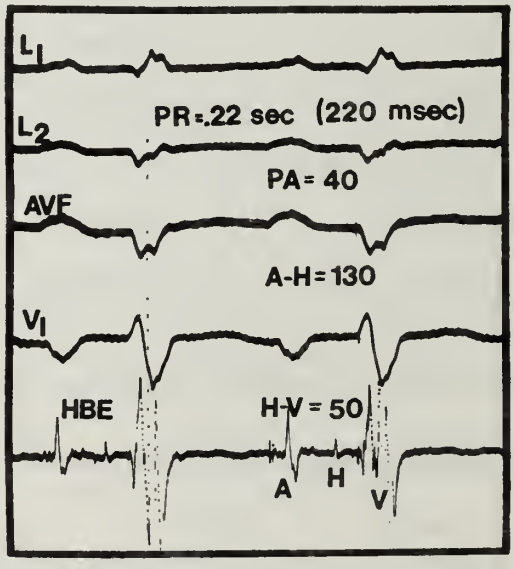


Fig. 5: *Case 3 - His bundle recordings 15 days after the acute myocardial infarction. The P-A and H-V intervals are within normal limits. The A-H interval is slightly prolonged. The PR interval is 220 msec.*

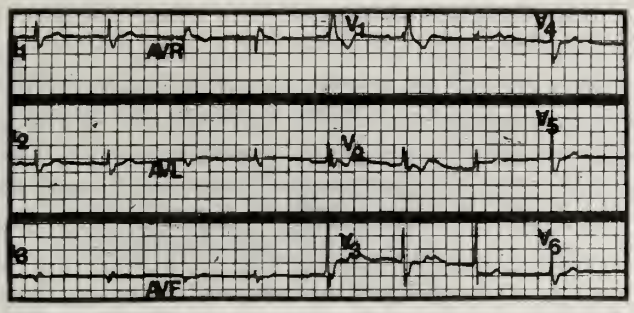


Fig. 6: *Case 3 - Electrocardiogram taken at the time of admission. Complete RBBB, left axis deviation and first degree A-V block are present. The sinus rate is 56 per minute.*

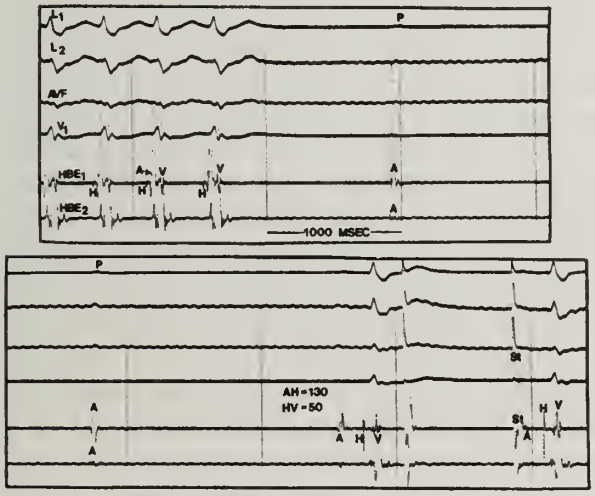


Fig. 7: *Case 3 - Reciprocating A-V junctional tachycardia observed at the time of the His bundle recordings; the strips are continuous. The low right atrial electrogram was lost within the ventricular deflections of the HBE lead. Immediately after the termination of the tachycardia, there was a period of A-V block during which the atrial deflections failed to activate the His bundle.*

recordings seem to be of value in determining the short term prognosis in this group of patients. The prognosis is poor for those with prolonged H-V intervals and persistent RBBB and better for those with a normal H-V interval and transient RBBB. Although it has been suggested that persistent right bundle branch block with left axis deviation in acute myocardial infarction might be an indication for permanent cardiac pacing (23, 27) further observations and controlled studies are required to validate this statement.

Considering the delayed onset and transient nature of the bundle branch block associated with a normal H-V interval (at the time of the second HBE), it is reasonable to conclude that prophylactic permanent pacing was not required in the case presented.

It is possible that serial measurements of H-V intervals during the acute stage would identify a sub-group of patients that might benefit from a permanent pacemaker. More patients with acute myocardial infarction complicated by incomplete bilateral bundle branch block need to be followed up for longer periods of time to determine the effect of such intraventricular conduction disturbances on ultimate prognosis.

Case 3: This 69 year old male was followed in the outpatient clinic because of RBBB, left axis deviation and first degree A-V block (Figure 6). He was admitted for evaluation because of dizziness and fainting spells. There was no history of hypertension, diabetes or coronary artery disease. The results of the physical examination were unremarkable except for the presence of a fourth heart sound. Neurologic work up was negative. Brain scan and flow studies were suggestive of decreased blood flow in the area supplied by the right middle cerebral artery. Several 24 hours Holter monitoring studies were normal except for sinus bradycardia (56/minute).

Electrophysiologic Studies:

During sinus rhythm at a rate of 60 per minute, the A-H and H-V intervals were 130 and 50 msec respectively. During atrial paired pacing, the patient developed reciprocating A-V junctional tachycardia (Figure 7) at a rate of 150 beats per minute. The arrythmia terminated spontaneously. Immediately after the end of the tachycardia there was a period of A-V block during which the atrial deflections apparently failed to activate the His bundle. The corresponding P-P interval preceding the first conducted sinus beat measured 1640 msec. The prolonged duration of this interval suggested the coexistence of sinus node dysfunction. During this episode, which occurred in the Cardiovascular Laboratory, the patient developed symptoms which were similar to those that he experienced before admission to the hospital. Three explanations appeared possible to explain the symptomatic post tachycardia A-V nodal block: (a) post tachycardia induced period of abnormally prolonged A-V nodal refractoriness; (b) pseudo A-V block produced by concealed A-V junctional tachycardia and (c) bradycardia-dependent (phase 4) A-V block at the "upper" His bundle (28).

A permanent pacemaker was recommended because reciprocating A-V junctional tachycardias occurred in a symptomatic patient with sinus node dysfunction. Digoxin was given in an attempt to prevent the tachyarrythmias. He has been asymptomatic for 10 months.

Comments:

The reported incidence of development of heart block in patients with bifascicular block, especially right bundle branch block and left anterior hemiblock has ranged from 6 to 30 percent over a period of several months to several decades (15, 16, 29). A recent prospective study on the natural history of these patients showed that progression of conduction disease was uncommon, occurring in only 6 per-

cent of patients during a mean follow-up period of 1 1/2 years (30). In this series, patients with both normal and prolonged H-V intervals had a relatively high incidence of sudden cardiac death which could have been secondary to progression of conduction disease or ventricular fibrillation (30). Watanahe et al (31) recently reported a higher incidence of ventricular arrhythmias in patients with intraventricular conduction defects than in patients with normal intraventricular conduction and when these are subjected to graded exercise, they manifest premature atrial and ventricular beats and occasionally ventricular tachycardia (32). In the case presented, symptoms could have been due to complete A-V block or to ventricular tachycardia. Sinus node dysfunction and reciprocating A-V junctional tachycardia were not suspected to be the contributing factors accounting for his clinical presentation. The information derived from His bundle electrocardiography was useful in the management of the patient and provided possible mechanisms which could be useful in understanding the genesis of symptomatic post tachycardia A-V block in patients with tachycardia-bradycardia syndrome.

Discussion

His bundle electrocardiography has been primarily considered a research technique useful in studying the conduction system of the heart and the effects of pharmacologic and physiologic interventions on A-V conduction. At the present time there are several clinical situations where critical information can only be obtained through His bundle recordings. As demonstrated in Case 1, His bundle recordings appear to be of clinical value in patients with neurologic symptoms and bundle branch block. Scheinman et al (19) reported three groups of patients with bundle branch block, dizziness, seizures or syncope and the presence of 1:1 antegrade A-V conduction at the time of the His bundle recordings. None of the patients studied had evidence of an acute myocardial infarction. In six patients neurologic symptoms were observed in the absence of electrocardiographic evidence of A-V block. The H-V interval in this group of patients was normal or minimally prolonged (mean 56 ± 9). In six other patients, the cause of the symptoms was not clear, however, in three patients the symptoms were of sufficient concern to merit implantation of a permanent cardiac pacemaker. Two of these patients experienced relief of symptoms suggesting that they were in fact related to transient bradyarrhythmias. The mean H-V interval in this group was 64 ± 11 msec. In seven other patients complete A-V block was documented as the cause of the symptoms. The H-V interval was significantly prolonged in every patient, with a mean value of 89 ± 20 msec. All patients with presumed or documented episodes of high grade A-V block had abnormal H-V intervals and six of the nine patients had H-V intervals over 80 msec. The significantly greater H-V interval in patients with documented A-V block, suggested that the specialized ventricular conduction system is involved in a progressive disease process the end stage of which results in complete A-V block (19). On the other hand, previous studies have demonstrated that a normal H-V interval in patients with bundle branch block does not preclude development of complete A-V block (33). In view of this, it remains to be determined if His bundle electrocardiography can provide a means to quantitate A-V conduction disturbances.

The indications for permanent cardiac pacemakers after an acute myocardial infarction remain a controversial issue (16, 23, 27, 34). Atkins et al (27) reported 16 patients with acute myocardial infarction and RBBB-LAD. Twelve patients had complete heart block in the first 48 hours, one of these patients died and 11 were temporarily paced. The pacemakers were removed in 7 of the 11 patients after reversion to sinus rhythm. Eight patients died suddenly and unexpectedly between 2 weeks and 4 months after the infarction. Seven of these had transient heart block during the acute stage and 3 patients had documented recurrent complete heart block. On the basis of this data they suggested that persistent RBBB with LAD in acute myocardial infarction might be an indication for permanent pacemakers. Later Scalon et al (16) and Godman et al (22) described seven patients with RBBB-LAD who had transient complete heart block during an acute myocardial infarction; six of these patients died within eight months. Considering these reports and in view of their previous experience, Atkins et al (23) later restricted their recommendation to the group of patients with persistent RBBB-LAD who had developed transient complete A-V block during the acute stage of myocardial infarction. They found that 11 of 13 patients who did not have a permanent pacemaker died within 8 months of discharge, whereas 8 with permanent pacemakers were still alive. The possibility that sudden death might have been secondary to ventricular fibrillation during an acute ischemic episode was considered in a recent reappraisal of their report (34). At the other end of the spectrum, Waters and Mizgala (34) recently reported their experience with 27 patients with acute myocardial infarction complicated by incomplete bilateral bundle branch

block, treated with temporary transvenous pacemakers. Twelve of the 27 patients died in the hospital. Progression to complete heart block occurred in 9 of the 12 patients. Fourteen of the 15 survivors have been followed up an average of 16.7 months after infarction and one had developed complete heart block. In 7 of the survivors, follow up studies indicated a trend toward regression of the conduction disturbances. The authors did not believe that the occurrence of transient complete heart block in patients with an acute myocardial infarction complicated by incomplete bilateral bundle branch block is an indication for permanent pacemaker insertion. In view of these conflicting observations it is reasonable to examine the value of His bundle electrograms in relation to the short term prognosis in this group of patients. In the series reported by Lichstein et al (20) and Lie et al (26), His bundle recordings were made in 50 patients at the time of temporary pacemaker insertion. Twenty-one of the 27 patients with bifascicular block and prolonged H-V interval died in comparison to ten deaths in 23 patients with bifascicular block and a normal H-V interval. A very interesting observation can be made by analyzing the data reported by Lichstein et al (20). Of the patients with an abnormal H-V interval (55 msec or greater) 8 died and 3 survived. In this group, there were 5 patients with H-V intervals of 70 msec or greater (range 70-100 msec), all of them died. All of the 6 survivors had H-V intervals less than 70 msec (range 45-65 msec). Although further observations and controlled studied are needed, this preliminary data suggests that His bundle recordings provide an important tool that might be used to quantitate A-V conduction disturbances. Whether permanent cardiac pacing is indicated in the group of patients with abnormal H-V intervals remains to be determined.

As we expand our understanding of the pathophysiology of conduction disturbances and cardiac arrythmias, the information derived from His bundle recordings will become more useful in the management of patients with intraventricular conduction disturbances.

Summary

His bundle electrocardiography has enhanced our understanding of arrythmias, the WPW syndrome and the site of conduction abnormality in patients with heart block. However, the usefulness of this procedure in the routine care of cardiac patients has been questioned. Three cases are presented to illustrate the potential and practical value of His bundle recordings in the evaluation and clinical management of patients with conduction disturbances.

Acknowledgment

We would like to acknowledge Benjamín Scherlag, Ph.D. for his helpful criticism and the cooperation of Miss Bonnie Agnell for the typewritten preparation of the manuscript.

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MANEJO DEL COMA HEPATICO AGUDO

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La encefalopatía hepática aguda es por definición el complejo de síntomas neuropsiquiátricos que vemos asociado a la insuficiencia hepática. Usamos esta definición tan general ya que la variabilidad de este síndrome es muy grande, desde el daño mínimo al sensorio e intelecto que vemos en cirrosis crónica, al delirio rápido, convulsiones, y coma que ocurre en necrosis hepática fulminante. Es precisamente este coma catastrófico el que queremos discutir, ya que su dificultad de manejo es notoria, y su pronóstico, sombrío.

Presentación Clínica

Los hallazgos clínicos en el coma hepático usualmente reflejan la multiplicidad de causas y factores precipitantes. El paciente puede manifestar cambios asociados con malnutrición tales como glositis, pérdida de peso, e inanición. Si la causa es cirrosis crónica podemos ver cambios endocrinos tales como telangestasias, eritemas, angiomas abdominales, alopecia y atrofia testicular. Distensión abdominal, ascitis, y diástesis hemorrágicas pueden verse en casos severos. Fiebre ocurre con frecuencia en los casos fulminantes.

En los estadíos tempranos del coma agudo podemos ver disturbios en intelecto y sensorio: confusión, defectos en juicio, depresión, euforia. Luego vemos inquietud, alucinaciones, insomnio, delirios y convulsiones. Asterixis, aunque característico, puede verse en otros desórdenes también.

Usualmente se acompaña el cambio en comportamiento por cambios en el electroencefalograma. Gradualmente se pierde el patrón normal de alta frecuencia (alfa), y se desarrollan ondas de alta amplitud y baja frecuencia (delta). Sin embargo, estos cambios pueden también verse en otras condiciones como insuficiencia pulmonar, uremia, anemia, intoxicación alcohólica, hipocalcemia, sueño profundo, anestesia, hipoglicemia, intoxicación por barbitúricos, y narcosis de CO_2.

Sangramiento gastrointestinal de várices esofágicas, gastritis o úlcera péptica son factores precipitantes bastante comunes. Hipoxia y shock después de sangría o infección son también factores de importancia, al igual que infecciones, peritonitis y sepsis. Morfina, sedantes, y desbalance electrolítico también pueden precipitar el coma.

Cambios Bioquímicos:

Disfunción hepática resulta en disturbios metabólicos a todos los niveles, variando los cambios con la severidad de la enfermedad, su etiología, y los factores precipitantes. Cambios ocurren en el metabolismo de carbohidratos, lípidos, proteínas, encimas hepáticas, y factores de coagulación. El amonia arterial está aumentando en la mayoría de los casos, pero no es consistente ni uniforme. Acidosis metabólica ocurre en los estadíos tempranos del coma asociado con necrosis extensa. En contraste, el uso paralelo de diuréticos con frecuencia resulta en alcalosis metabólica, la cual magnifica el efecto de la alcalosis respiratoria que es causada por la acción de "toxinas" en el centro respiratorio. Hay cambios universales en aminoácidos en sangre, orina, cerebro, y líquido cefalorraquídeo. Transaminasas, bilirubina, y fosfatasa alcalina están alteradas dependiendo del grado de reserva hepática. Las proteínas totales están usualmente disminuídas.

A pesar de que los siguientes cambios no son consistentes y su determinación rutinaria es difícil, ocurren variaciones en otros metabolitos importantes tales como la acetoína, glicol butilénico, sales biliares, ácidos grasos, fenoles e indoles, hormonas, deaminasas, aminopeptidasas, y otros.

Terapia

Manejo General:

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Este trabajo fue llevado a cabo con ayuda de USPHS General Research Support Grant No. 5-S01-RR-05419-13 y NIH Special Fellowship No. 1-F03-Am51611-01.

En primer lugar es importante que se reconozcan los factores precipitantes en el manejo inicial de estos pacientes. Se debe eliminar la injesta de nitrógeno exógeno al igual que controlar otras fuentes tales como hemorragia. Shock debe ser evitado a toda costa, y si ya está presente, debe ser manejado vigorosamente. Se debe ejercitar mucho juicio en el uso de diuréticos para evitar inducir un desbalance electrolítico. De hecho, si posible no deben usarse. Aún si hay ascitis, una paracentesis lenta y pequeña resulta mejor que el uso injuicioso de diuréticos. El manejo y la búsqueda de toda posible infección debe ser una consideración primaria en el manejo total del paciente. El paciente debe ser manejado en una unidad de cuido intensivo con observación cercana de parámetros fisiológicos y metabólicos, y con cuido intensivo de enfermería.

La literatura está repleta de modalidades de manejo, algunas de las cuales son de mucho valor, y otras que gradualmente han sido descartadas. En términos generales se pueden dividir en "terapia metabólica" y "terapia extracorpórea". Tratamientos metabólicos importantes incluyen: el intento de disminuir la absorción y concentración de amonia con arginina y glutamato, y ácido aspártico; el uso de drogas neurotrópicas tales como L-Dopa; los esteroides adrenales. Vías extracorpóreas de manejo hepático incluyen: hemoperfusión de la sangre del paciente por resinas de intercambio de iones, diálisis peritoneal, hemodiálisis, exsanguíneo-transfusión, plasma exanguineo-transfusión, perfusión hepática ex-vivo heteróloga, circulación cruzada, diálisis cruzada, y trasplante hepático. Algunas han sido incorporadas a las guías de terapia que sugerimos a continuación.

Manejo Específico

I - Propósitos Generales y Objetivos:

A. Principios Generales:

1. Determinación y tratamiento de la etiología.
2. Determinación de la severidad del déficit hepático.
3. Determinación de la severidad de destrucción y necrosis tisular, si presentes.
4. Determinación del impacto en la homeostasis total.
5. Detección de factores precipitantes, si alguno.
6. Sustitución temporal de las funciones hepáticas principales.
7. Remoción o inactivación de substancias nocivas.

B. Objetivos Específicos:

1. Eliminar y tratar los factores precipitantes.
2. Corregir volumen y electrolitos.
3. Corregir problemas de coagulación.
4. Limpiar el tracto gastrointestinal.
5. "Esterilizar" el tracto gastrointestinal.
6. Detener el sangramiento intestinal si presente.
7. Remover e inactivar las toxinas circulantes.

II. Manejo Específico:

A. Observación y seguimiento:

1. El paciente debe estar en una unidad de cuido intensivo.
2. Catéter vesical y medición de orina cada hora.
3. Succión nasogástrica; irrigar periódicamente para mantener completamente limpio.
4. Medir toda ingesta y débito.
5. Medir presión venosa central, presión arterial, pulso y respiración cada hora o más frecuente.
6. Monitor de electrocardiograma y de presión constante.
7. Peso diario.

B. *Pruebas Diagnósticas:* Se han de medir los niveles de las siguientes sustancias con frecuencia y de modo secuencial:

1. Hematocrito, azúcar, pH, pO_2, pCO_2.
2. K, Na, Cl, HCO_3, Ca, Mg, PO_4.
3. Albúmina; si posible, electroforesis.
4. Fibrinógeno, contaje plaquetario, PT, PTT, PRT, tiempo de lisis de euglobulinas, productos de degeneración de fibrina.
5. Urea, creatinina.
6. Bilirrubina, SGOT, SGPT, fosfatasa alcalina, amonia arterial.
7. Cultivos de sangre seriados.
8. Osmolaridad en suero y orina.
9. Examen neurológico por lo menos dos veces al día.
10. Electroencefalograma seriado.
11. Punción lumbar en casos nuevos o dudosos. Si posible hacer niveles de glutamina en el líquido cerebroraquídeo.
12. Parecentesis diagnóstica o terapéutica re-

cordando remover tan solo cantidades pequeñas (de dos a tres litros) lentamente.

13. Si hay sangría generalizada diferenciar entre actividad fibrinolítica aumentada, déficit de factores de coagulación, y coagulopatía por consumo.

C. *Medicamentos:*

1. Neomicina 1 gm cada hora por el tubo nasogástrico, x 4 veces y luego 1 gm cada 4 horas.
2. Leche de magnesia 60 ml oral stat, y 30 ml cada 4 horas por 24 horas.
3. Enemas altas hasta que salga claro, y luego cada 6 a 12 horas. Añadir neomicina a las primeras tres o cuatro enemas.
4. Cefalotin 1 gm IV cada 6 horas.
5. Oxígeno por máscara, de 6 a 8 L/min; considerar recirculación si hay alcalosis.
6. Sulfato de magnesio 50 por ciento, 1 a 2 ml IM profundo cada 8 a 24 horas según sea necesario para controlar niveles de magnesio e irritabilidad muscular.
7. Cloruro de calcio 10 por ciento - 10 cc IV despacio cada 8 a 24 horas para controlar la hipocalcemia, especialmente en presencia de alcalosis e hipoalbunemia.
8. Glutamato de arginina, 50 gm IV stat y 25 gm IV cada 6 a 8 horas en 250 ml de glucosa al 10 por ciento.
9. Sueros intravenosos cristaloides: de 1,500 a 2,500 ml, Na Cl en D5W o D10W, dependiendo en la concentración de electrolitos y glucosa. Añadir las vitaminas correspondientes.
10. Añadir de 60-80 MEq/L de KCL a los sueros para corregir la hipokalemia.
11. Albumina, 25-75 gm diarios dependiendo de los niveles.
12. Sangre completa y/o células lavadas para reemplazar pérdida sanguínea. Debe ser lo más fresca posible para proveer factores de coagulación y para disminuir la carga de amonia.
13. Vitamina K 50 mg IV despacio el primer día, y 20 mg IV diario.
14. Si se hace imprescindible el uso de diuréticos, úsense con extrema cautela. Espironolactona sola o en combinación con furosemida pueden ser de valor.
15. Sedación: Benadryl 25-50 mg IM cada 6-8 horas. No usar narcóticos, barbitúricos, o sicomiméticos.
16. Digitalización si necesario. Seguir niveles de potasio sérico por lo menos una vez al día.

D. *Control de sangramiento gastrointestinal:*

1. Lavado gástrico vigoroso con salina helada.
2. Esofagogastroscopía inmediata para diagnóstico.
3. Pitresina 20 unidades IV en 10 a 20 minutos, midiendo de cerca los signos vitales. Se puede repetir en una o dos horas.
4. Tamponada gastroesofágica con el tubo de Zengstaken.
5. Si el sangramiento es por gastritis o úlceras, dar levarterenol 16 mg en 200 ml de salina via tubo nasogástrico. Ocluir el tubo por 30 minutos. Puede repetirse en ciclos de 30 minutos por dos o tres veces.
6. Si el sangramiento es por várices, infusión intraarterial selectiva esplánenica de vasopresina.
7. A pesar de todos los esfuerzos, cirugía puede ser inevitable.

E. *Si el coma persiste o empeora:* Considérese entonces las siguientes modalidades pero tan solo bajo supervisión estricta y circunstancias controladas:

1. L-Dopa por tubo nasogástrico. Comenzar con 250 mg y aumentar la dosis al máximo de 50 mg/kg/día en dosis divididas. Terapia por más de 3 o 4 días puede producir irritación gástrica.
2. L-Dopa IV: 0.1 por ciento solución en 0.9 por ciento salina. Dar de 600 a 1,200 mg por día IV despacio por 3 a 5 días.
3. Esteroides en dosis masivas (30 mg/kg como en shock séptico) en casos con sepsis o necrosis hepática masiva. Darlo en una sola inyección despacio (5-10 minutos). Puede repetirse en 4 horas.
4. Exanguineotransfusión.
5. Diálisis peritoneal.
6. Hemodiálisis.
7. Perfusión hepática ex-vivo, hemoperfusión por resinas, circulación cruzada, diálisis cruzada, e hipotermia con hemodilución tan solo pueden ser intentadas bajo condiciones protocolarias formales, en centros grandes y por equipos altamente entrenados.

MEDICINE AND THE CRISIS IN CONFIDENCE

Edward H. Reinhard, MD

I would like to consider the confidence crisis that confronts us under two headings: first from the standpoint of tremendous events which have occurred during the last twenty years that have profoundly influenced the mechanics of the delivery of medical care and the interplay between patients and the medical "system", especially as we know it in a large medical center; and second, from the standpoint of the relationship of the individual physician and the patient.

In order to understand the historical events which underlie the confidence crisis which now confronts the medical profession, it is necessary to consider the truly astonishing scientific revolution which during the last 100 years has converted medicine from little more than witchcraft into a highly complex science. We tend to forget that 130 years ago the average doctor had little to offer other than crude surgery, and purging, puking and blood letting, which often shortened rather than prolonged the patients' lives. But even more astonishing than the emergence of medicine from the age of witchcraft has been the more recent, every increasing explosion of scientific knowledge which has occurred during our lifetime. It is a sobering experience to stop for a minute and consider the scope and magnitude of this explosion. Some of the more important areas in which revolutionary new concepts have emerged include the elucidation of intracellular coding and the recognition, "computerization" and transferral of genetic information that occurs during cell division; new information on the biochemical pathways involved in the development of the energy required for cellular metabolism; metabolic control and feed-back mechanisms involved in a host of cellular and organ functions, the nature and function of subcellular organelles, the role of cyclic AMP, the complex physiology of renal function, the mechanisms of transport of inorganic and organic molecules across cell membranes and the elucidation of antigen-antibody reactions and cellular immunity, to mention just a few of the tremendous advances in our knowledge of cellular and organ function.

In addition to these great advances in basic science knowledge at the biochemical, physiological, cellular and organ levels, there have also been startling advances at the clinical level. Consider the spectacular improvements in the treatment of infectious diseases. When I was an intern bacterial endocarditis was still a highly lethal disease because, although penicillin had just been discovered, its availability was limited and it was used in totally inadequate doses by present day standards. The only treatments for tuberculosis were bed rest, pneumothorax and surgical collapse of the lung. The artificial kidney was unknown and renal failure meant almost certain and prompt death. Open heart surgery had not been considered. In our simplicity and ignorance we never dreamed of the avalanche of potent and, at times, toxic drugs which are now available to correct aberrations in physiological function, to soothe those who are agitated, to "elevate" those who are depressed, to kill cancer and leukemic cells, and, at times, to interact with other drugs to the detriment of the patient.

Indeed, it can be said that we are in the midst of the golden age of medicine from the standpoint of scientific accomplishment. This being so, one would suppose that our profession as a whole and we, as individual physicians, should be regarded by at least a majority of people with respect, if not with reverence. No physician is naive enough to believe that this is so. One has only to read the extraordinarily candid remarks of Senator Edward Kennedy to appreciate that we are considered money mad, selfish, and often even incompetent to translate existing medical knowledge into optimum medical care. One may dislike Senator Kennedy, but there can be little doubt that he is an astute and experienced politician

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Presented at the 73rd Annual Meeting of the Puerto Rico Medical Association, Caribe Hilton, 11/21/75.

who would not make such public comments unless he was convinced that his remarks would fall on sympathetic ears. One could comment that the Senator himself belongs to a "profession" which is held in even lower regard than the medical profession at present, but I find no comfort in this fact.

Direct attacks on the medical profession are unpleasant enough, but even more difficult to deal with is biting ridicule as exemplified by a recent *Code of Ethical Behavior for Patients* published in Saturday Review (1). I quote part of this:

DO NOT EXPECT YOUR DOCTOR TO SHARE YOUR DISCOMFORT

Involvement with the patient's suffering might cause him to lose valuable scientific objectivity.

BE CHEERFUL AT ALL TIMES

Your doctor leads a busy and trying life and requires all the gentleness and reassurance he can get.

TRY TO SUFFER FROM THE DISEASE FOR WHICH YOU ARE BEING TREATED

Remember that your doctor has a professional reputation to uphold.

DO NOT COMPLAIN IF THE TREATMENT FAILS TO BRING RELIEF

You must believe that your doctor has achieved a deep insight into the true nature of your illness, which transcends any mere permanent disability you may have experienced.

DO NOT SUFFER FROM AILMENTS THAT YOU CANNOT AFFORD

It is sheer arrogance to contract illnesses that are beyond your means.

NEVER REVEAL ANY OF THE SHORTCOMINGS THAT HAVE COME TO LIGHT IN THE COURSE OF TREATMENT BY YOUR DOCTOR

The patient-doctor relationship is a privileged one, and you have a sacred duty to protect him from exposure. Etc.

Why is there this startling discrepancy between the unprecedented and spectacular achievements of medical scientists in the conquest of disease and the low regard in which our profession and we as individuals physicians are held? I would like to explore the idea that some of the legitimate criticisms that are levelled against the medical profession are direct *results* of the success which medical scientists have achieved in improving the treatment of disease and in offering the reasonable expectation that in the future there will be progressively increasing progress in combatting both organic and functional disorders which render people ineffective human beings. This may sound paradoxical, but the paradox derives from the fact that medical science and medicine are not the same thing. Medical science is science *in* medicine; medicine itself is a broader thing, a discipline at the interface of science and human need. Medicine involves interactions between human beings and requirements which cannot be met through scientific advance alone.

With this definition of medicine in mind, I would like to consider some of the complaints levelled against our profession by patients which seem to me to be legitimate and which are directly the result of the information explosion. Certainly, no one can possibly doubt that the delivery of optimum medical care is absolutely dependent on the proper and efficient application of present day medical knowledge to clinical problems, that medical science is the foundation upon which all clinical effort rests, and that further advances in medical care are clearly dependent on a steady expansion of knowledge in the basic sciences and medical science. However, as a result of the vast increase in medical knowledge which has already occurred, and the availability of increasingly accurate and effective, *but also increasingly complicated* diagnostic procedures, the care of the individual patient is becoming ever more complex and depersonalized. In community hospitals many, if not most, patients are now cared for by two or more physicians, each handling problems in his or her own specialized field of interest. If it were not so, it would be impossible to bring to bear on the clinical problems the best and most up-to-date information, as no one physician can possibly have at his fingertips detailed data about recent advances in knowledge in all the subspecialties of medicine. In a large medical center, in addition to this often impressive list of consultants, the patient is seen, examined and interacts with numerous house officers, fellow, and, perhaps, medical students. This multiplicity of doctors often persists after the patient is discharged. He or she may continue to be followed by an internist and a psychiatrist, in addition to occasional visits to an ophthalmologist,

a dermatologist, and perhaps a yearly visit for the female patient to a gynecologist for a pelvic examination and a Pap smear. This fragmentation makes it enormously difficult to provide the patient with long term, comprehensive, unified medical care. The internist or family physician may not probe into the patient's personal life, because he knows this individual is seeing a psychiatrist regularly, but proper understanding and treatment of the troublesome diarrhea may be impossible, unless the internist is aware that the patient's wife is an alcoholic or that he is obsessed with anxieties about his sex life or his business. The problem is further complicated as the patient grows older, by the accumulation of more and more past illnesses and permanent disabilities which might have a bearing on the present illness. A thick dossier accumulates and, unfortunately, in our nomadic society where many families never live more than 4 to 5 years in any one place, the dossier is often spread over many localities. A new physician seeing the patient for the first time may be overwhelmed by the magnitude of the job involved in getting all of the available data about the patient toegther in one place. If the patient has an illness such as diabetes, rheumatoid arthritis, hypertension or arteriosclerosis, there is a tendency to ascribe new complaints to the old disorder, and new organic diseases and overwhelming personal events which are responsible for new symptoms, may be ignored.

At this point I would like to dramatize these abstract considerations by considering a hypothetical 50 year old woman from Prairie Junction, Missouri, who has the misfortune to run a fever for 5 weeks. Her family physician finds no obvious cause for the fever, and he becomes concerned that the FUO may be a manifestation of some serious, underlying disease, so he refers her to Dr. Patrick Spratt at a large medical school affiliated hospital. First the patient suffers the trauma of waiting for several hours in the waiting room while the halt, the lame and the blind swirl around her like a prairie dust storm. She is finally admitted and arrives in her hospital room at 4 PM. An intern takes a history and examines her at 7:30 PM. She doesn't really have any symptoms except "fever", but on specific questioning she admits to recent headaches, occasional indigestion, and slight weight loss. Her hemoglobin is 11.5 grams. At 10 PM the assistant resident takes another history and examines her again. Dr. Spratt and then a medical student repeat the process the following morning. During the ensuing 3 weeks the patient has 10 blood cultures, a spinal puncture, chest x-rays, and an upper and then a lower gastrointestinal x-ray examination, both carried out with an almost total lack of privacy in surroundings that resemble Omaha Beach at the time of the Allied invasion. Every orifice of her body including the most private ones are examined with minute care. Minimal neurological findings have been detected and consequently an electroencephalogram, skull films, and finally an EMI test are performed. The confused patient makes the mistake of asking the intern what an EMI test is. The intern replies, as he dashes out of the room, that EMI refers to Electrical Musical Instruments, the name of the company that makes the computerized x-ray monster. At the end of the second week in the hospital the patient mails a letter to her husband in Prairie Junction about her experiences in the hospital, and she encloses the bill which was placed on her bedside table while her spinal puncture was being performed. Three days later her husband is sitting in a rocking chair smoking a pipe and staring out over his cornfield with the hospital bill in his hand. He is staggered by the amount of the bill, but, in particular, he is trying to figure out what could possibly have been done on the Electrical Musical Instrument machine that could conceivably cost $225. The patient in the other bed in the two-bed unit is desperately sick and is attached to a cardiac monitor. Two days after our patient's admission, the other patient has a cardiac arrest and something called Code 7 is announced over the speaker system. The marines storm in dragging their howitzers and gas tanks and all the paraphernalia of the wars against death behind them. It is to no avail, and the patient dies. The curtains are pulled, but it is very obvious an hour later that a bed that was occupied by a human being is now cold and empty. The patient remains depressed for the next twenty-four hours. She becomes very confused by the number of doctors who come in to see her, so she keeps a record. When she leaves the hospital, as nearly as she can figure it out, she has been seen by Dr. Spratt, an infectious disease specialist and his three fellows, a gastroenterologist and his two fellows, a hematologist and two fellows, a neurologist, an intern, a resident and a medical student. She has been presented on teaching rounds attended by more physicians than there are in the entire county where she lives. Unfortunately, on the day she is discharged, Dr. Spratt has left the city to attend a medical meeting and she gets her final instructions from

Dr. Spratt's associate, whom she has never seen before. However, it is of little consequence because the fever is still of unknown origin and the student nurse could have given the instructions, which are to "keep in touch with your family physician". A month later bills begin to arrive from the medical specialists. The patient tries to connect the bills with the individuals. By now they are all a blurr of unfamiliar faces. She wonders if this bill is from the fat doctor with the black mustache, or is it from the tall, skinny doctor with the flowing white coat. It is all very confusing. Now this is obviously an exaggeration, but there is enough truth in this little account so that it hurts. What I am trying to emphasize is that as medical knowledge has increased by geometrical proportions, medical care of an individual patient has become enormously complex and the Alice-in-Wonderland experience we put patients through and what it costs is baffling and traumatic.

The idea that doctors are greedy and overpaid is subtly nurtured by items in the daily press such as the article in the Post-Dispatch (2) which stated "Five doctors at Southern Illinois University's School of Medicine at Springfield are paid more than $50,000 a year ----. They are among the state's highest paid employees: Governor Daniel Walker earns $50,000 a year. ---- 17 of the 20 highest paid state employees are administrators or faculty members at state medical schools ----." Can anyone doubt that the dissemination of such information creates resentment and hostility in the mind of a patient who has to borrow money to pay crushing medical bills for a catastrophic illness. During the 30 years that I have been on the faculty of Washington University Medical School, it has been fascinating watching the unfolding careers of young physicians after completion of their residency and fellowship training. Until fairly recently a typical house officer lived in a run-down apartment in a condition of real poverty until he entered medical practice. Thereafter, his income increased very rapidly, but, often, his financial responsibilities increased even more rapidly and 10 to 20 years later he found himself under constantly increasing pressure to increase his income still further in order to keep up with the cost of private schools and colleges, big cars, expensive vacations and all the ramifications of the affluent life often deemed essential to maintain a social status appropriate to a successful professional person. With increasing income, debts and anxieties about financial problems tend to increase rather than decrease. The old problem of "keeping up with the Jones" is not a joke - it is very real. There is a principle, known to me if to no one else, as Reinhard's principle, which states that if you wish to achieve peace and freedom from financial worry, buy a house in an old, modest neighborhood, a neighborhood which is shunned by the captains of industry, a neighborhood, where *you* are Jones. Let your neighbors worry about keeping up with *you* and *your* family and not vice versa. This principle is based on a philosophy of life that is un-American, but it leads to peace and contentment.

Actually, physicians' fees account for a relatively small percentage of total medical costs. We all know that some patients are admitted to the hospital who could easily be taken care of as outpatients. Organized medicine should strongly encourage health insurance which pays for outpatient medical care, in order to remove the almost irresistible pressure to hospitalize a patient with a borderline illness, so that the expense will be borne by an insurance company, and we should also support pre-paid health plans for low and middle income groups. Furthermore, the number of drugs prescribed for a single patient is sometimes scandalous, and an expensive drug is often prescribed when a much less expensive drug would be just as effective. The cost of treating a 135 pound patient in Barnes Hospital with 500 mg./kg./day of carbenicillin, which would be an appropriate dose for certain severe systemic infections, is $144 per day *just for the drug.* An average course of treatment would last about 10 days, and the cost for the *drug alone* would be approximately $1,500.

So much for the medical care delivery system. Next, I would like to consider the accusation that Senator Kennedy has levelled at the medical profession, that a great many physicians are incompetent and do not keep abreast of advancing medical knowledge. Here again, this problem stems, in part, from the successes of medical science. About *400 years B.C.* Hippocrates said:

"The art is getting longer and longer,
the brain of the student not bigger and bigger."

About 2,300 years later, in 1972 A.D., Lukasiewicz (3) of the engineering faculty of Carleton University in Ottawa, Canada, wrote a fascinating article, the title of which was "The Ignorance Explosion: A Contribution to the Study of the Confrontation of Man with the Complexity of Science-Based Society and Environment." The gist of this article was that as human knowledge

expands, the amount of information available, but which we are ignorant of, expands proportionately. The first two *scientific* journals were founded in 1665: The Philosophical Transactions of the Royal Society of London, and the Journal des Scavans in Paris. Professor Lukasiewicz states that since 1760 the number of scientific journals has been increasing at a constant exponential rate, doubling every 15 years or increasing tenfold every 50 years. It has been estimated that in the last 200 years over 100,000 scientific journals have been founded, many of which have ceased publication. However, Zelikoff estimated that 50,000 scientific journals were being published throughout the world in 1968. Very early it became apparent that the mind of man could not handle this mass of data, and the first abstract journal was published in Germany in 1714. By 1963, 1,855 scientific *abstract* journals were being published. At the present time a worldwide comprehensive system for the dissemination of scientific information is being developed under the auspices of the United Nations. This plan, called the World Science Information System, envisages computer storage of all scientific information, machine translated into a common metalanguage which can then be retrieved in any desired language. In this explosion of scientific knowledge, medical science has certainly been at the forefront.

I am grateful that I have had the opportunity to be a part of this tremendously exciting period in medical history. I have no doubt that the next decade will be every bit as exciting as the last decade. However, it is obvious that it is now exceedingly difficult for any physician to "keep up" with the flood of new medical information.

Another serious problem which contributes to the erosion of the confidence patients have in their physicians derives from an unexpected source. The physician practicing medicine today often has to deal with a patient who has preconceived notions about how he should be treated and unrealistic expectations about the possibility of a prompt and permanent cure because he has been bombarded by radio, television and press accounts of new discoveries concerning diet and drugs in the treatment of disease, as well as a vast array of medical discoveries announced by research workers and public agencies. The individual patient is seldom qualified to judge the applicability of this information to his or her individual problems, but the pronouncements are often accepted at face value. Even more serious than this is the increasing intensity of drug advertising in the public news media. Smith (4) in 1972 monitored a commercial network television channel in Detroit during a typical 130 hour broadcast week. Only 30 percent of this health time offered useful information and 70 percent of the health material was inaccurate or misleading or both. Most difficult of all to deal with are the news reports in the mass media of dramatic cancer, arthritis or other cures that involve outright quackery. A good example of this is the furor about Laetrile, a substance made from apricot seeds, first promoted as a treatment for far advanced cancer by a group of doctors in California in 1920. Later the claim was made that an enzyme present in tumor cells released hydrocyanic acid from Laetrile and this stopped respiration in the tumor cell. Can you imagine a more dramatic way to do in a tumor cell. While it is true that when this substance gets into cells, minute amounts of cyanide may be released, the amount released is infinitesimal, and, more important, almost all normal cells contain the enzyme that releases cyanide and there is no selective action on malignant cells. Nevertheless, the drug was extensively used in the late 1950's and early 1960's, although it was never approved by the FDA or any other legitimate scientific authority. When it was banned in this country it fell into disuse. It then reappeared on the scene under the label of "vitamin B-17" and thus it was hoped it would not be subject to banning by the FDA. This ploy didn't work and its distribution was again forbidden. However, it has been used extensively at a "clinic" in Mexico, and a woman living in the St. Louis area appeared on television a year ago and gave a glowing account of how she was cured of breast cancer by this "new" wonder drug after having been told by her doctor at Barnes Hospital that she had metastatic breast cancer and had only a few months to live.

In dealing with a patient who demands Laetrile therapy or even some legitimate form of therapy which is not, however, appropriate for the particular patient, we have a tendency to be hostile and brusque. Why should we have to put up with this nonsense? There are two important factors to remember. First, the patient lacks the background and knowledge to permit him or her to properly evaluate the wild and exaggerated claims that have been made about the treatment, and, second, if the patient has a life threatening illness, grasping at straws is a normal, human reaction. There is no substitute for a detailed and time consuming explanation that the drug has

been carefully studied by several impartial groups of scientists who have found that it does not release cyanide selectively in malignant cells, and that in controlled studies in animals it has been shown to be no more effective than a placebo.

We have discussed numerous factors that influence what patients think about the medical profession, including depersonalization and fragmentation of medical care, the skyrocketing cost of medical treatment, doubts about the competence of large segments of the medical profession, and the role of the news media and drug advertising in creating false ideas and expectations as to what can reasonably be achieved. However, we must realize that it is not *really* these problems that have led to the crisis in confidence - rather, it is the way in which we (the medical profession) have reacted to them. Dag Hammarskjold has said:

"Is life so wretched?
Isn't it rather *your* hands which are too small,
Your vision which is muddied?
You are the one who must grow up".

In a sense all of these things which we have been discussing are intimately related to the topic which I have saved for last, as I believe it is the most important factor influencing the crisis in confidence. I am referring to the relationship between the doctor and the patient.

In May 1974 a conference was held in New York City under the co-sponsorship of two women's organizations. The topic was *Psychological Perspectives in Women's Medicine - Telling It The Way It Feels* (5). After talks by a panel of guest psychologists, gynecologists, science writers and others, the meeting was thrown open for discussion. According to a New York Times reporter, it turned out to be a day long gripe session. While a few of the women had kind things to say about their physicians, most of them were highly critical. One small, dark haired woman said, "I went to my doctor Thursday, and afterwards I walked a block, sobbing hysterically. There was great hostility because I dared to ask him a question about a drug he had prescribed. He said "Where did you get your M.D. degree? ' I said I read Consumer Reports." Under the threat of death, the woman said, choking back tears, "I will not go back to him".

From the day we graduate from medical school we are set apart. We are called "doctor", whereas everyone else is called Mr. or Ms. We are the Chosen People. There is a great tendency to develop a God Complex. Arrogance is a luxury physicians can no longer afford.

I hate the term "bed-side manner" because to me this implies that something akin to charisma, the ability to charm and inspire admiration in the patient, is what we are seeking. Nothing is farther from the truth. To me, the essence of an ideal doctor-patient relationship is a quality that is hard to define, but can be illustrated. I would like to give an illustration.

This patient was a woman in her early 40's who I had seen half a dozen times before. She had gastrointestinal complaints and a mild anemia which seemed to be due, in part at least, to iron deficiency. She initially responded to iron therapy, but her hematocrit then levelled off at about 70 percent of normal, in spite of more than adequate iron therapy. One of the hematology fellows saw her and then came into my office to discuss the problem with me. His first statement was: "This patient is crazy". The patient had what we refer to in medical vernacular as a positive system review - she not only had every symptom in the book, but many of these symptoms were described in bizarre terms. I readily agreed that she was, indeed crazy - a classical example of what is often referred to as a "crock". I concentrated my attention on trying to decide what to do about my small fragment of "responsibility" for her total care - i.e. what to do about the anemia. After I had examined her, my fellow saw her again and carefully explained to her that her overwhelming fatigue could not possibly be due to her inconsequential anemia, and that her fatigue and most of her other symptoms appeared to be related to nervousness and anxiety. Apparently, he inspired a confidence in her that I had been too busy to encourage. She opened the flood gates and recounted an amazing story of a life undergoing total disintegration. Her husband had been admitted to a mental institution with little prospect that he would ever be released. She had no family and no close friends. Her financial situation had deteriorated from affluence to abject poverty. In a desperate effort to support her family, she enrolled in a school to get special training for a specific job. However, several months before she was scheduled to graduate she had a severe exacerbation of her gastrointestinal symptoms, which forced her to drop out of the school. She had 3 teenage children and she tried frantically to smile and joke when they were around, even though it was not clear where the money would come from to feed them in the future, and she had an overwhelming desire to hide in a closet and cry. And I, in my affluence and comfort, had done no better than to agree she was crazy. How would I have reacted to her insoluble problems? How would

you react? The haughty physician finds it so easy to dismiss the patient as a crock. It is so much more trouble, indeed it may be considered unmanly, to listen to the patient, to hear, to understand, to experience the terror. God forgive us for our arrogance.

Karl Gustave Jung has been quoted as saying "Only the hurt physicians can heal". Obviously any medical scientist can cure pneumococcal pneumonia by giving penicillin, but Jung was suggesting that healing in its broader context of restoring a sick and distraught person to wholeness requires a physician who has himself suffered, as only then can he really understand and experience the suffering of others. I suspect that there are some persons who achieve compassion without themselves having suffered greatly, but there is certainly an element of truth in Jung's statement. Many a brash, arrogant, over-confident young medical scientist who had difficulty when he first started to practice medicine developing empathy with his patients, eventually sees one of his own children injured in a devastating accident, or one of his children may get hooked on hard drugs, or his marriage may disintegrate, or he himself may suffer a catastrophic mental or physical illness. It is possible that out of the suffering and agony and from the depths of the black catacombs of despair through which he passes at this time, he may develop compassion - he may learn to understand the length and the breadth and the depth of hopelessness that some of his patients experience, not because they are dying, but because they are unable to cope with the fears, the anxieties, the ego crushing experiences of their lives, or perhaps because of the gradual realization that their lives are devoid of any real goal or meaning. He may learn that human illness is rarely the simple result of a bacterial or viral infection, an autoimmune reaction, the proliferation of malignant cells, or an endocrine or vascular disturbance. He will perceive that disease is a many faceted monster and that often the obvious organic disease, if there be such, is superimposed on a psyche in torment. He will be aware that the prolonged and expensive treatment he prescribes in the hospital may eradicate bacteria from the patient's spinal fluid and simultaneously destroy his financial integrity and the stability of his family. And when he has achieved this degree of understanding, *his patients will know* that he is aware of their torment, that he feels their pain, that he experiences with them the awful disruptiveness that disease can create in the human microcosm we call the family, and in the last hours, they will know that as death approaches he will not visit them less and less frequently for shorter and shorter periods of time. Rather, they will know that he will not be afraid or too busy to walk through the valley of the shadow of death with them; his touch, his presence, his candor will comfort them, they will not feel lost and alone, they will achieve acceptance, and when the final inpenetrable curtain is lowered they will depart from the stage in peace. In short, if he studies for the rest of his life, does not flaunt his superior status in life, shows humility, and, in addition, finally achieves the kind of understanding and compassion we have been talking about, there will be no lack of confidence; indeed, his patients will know that they are being taken care of not only by a competent medical scientist, but also by a great physician.

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THE HEART AND LA MORT D'AMOUR (MUERTE POR AMOR) SEX, SUDDEN DEATH AND THE HEART

Charles D. Johnson, MD

—the ancient power of fright and lust—
the female spider or the queen bee
whose embrace is death.
Robert Graves 1895—
The White Goddess 1948—ch 1.

—The stroke of death is as a lover's pinch,
which hurts, and is desir'd.
Shakespeare,
Antony & Cleopatra V, ii, 296.

—"and Cornelius Gallus, the Praetor, Tigillinus,
captain of the Roman watch, Lodowike, who was the
son of Guido Gonzaga, the Marquis of Mantua, end
their days between women's thighs? "
Montaigne (1533-1592) (1).

In contradistinction to the fruits and pleasures of sex (S) and love making, the participants in such may be liable to reap certain other hazards, other than illegitimate pregnancy and venereal diseases, nonetheless of which is sudden death (SD).

The black widow female spider (viuda negra) may sometimes devour or gobble-up the much smaller male after mating (a belief that gave her the name). Male bees, drones (zánganos) die or are allowed to starve-to-death after fertilization (2, 3).

Incidence

The "death of love" although recognized and imagined in song, prose, verse, works of art, legend, folklore and in the mundane experiences of human endeavors, has until recently received but insignificant cognizance in the realm of medical science. Its impact on the average physician has been regarded as essentially nil, being faced with only rarely in h s daily practice and work, but assuming a more familiar connotation in the practical experience and life spheres of coroners and medical examiners, and a few practitioners working in special places and circumstances. Due to the frequency of coital deaths (CD) in the US medical examiners have entitled it the "D.I.S." or Death in the Saddle Syndrome (4, 5).

Thus, in spite of what appears to be other than an extremely rare occurrence in the life of the populace and mankind, medical documentation likewise has been noteworthily almost nonexistent and no doubt underreported. This may be due to an understandable reluctance for revelation on the part of the main actors, supporting characters and members of the medical profession to divulge such dramatic events and tragedies. For the sake of social, moral, occupational, financial, marital, legal, familial and individual expediency, sorely needed medical facts and truths have only slowly been uncovered or yet lay buried on death certificates and medical statistics as more common and acceptable reasons for demise and departure from human flesh. "ASHD" has been a popular sign-out diagnosis for many cases of SD.

It has been generally accepted recently that the large increases in arterial blood pressure (BP) and heart rate (HR) may precipitate angina pectoris (AP) and "a relatively pleasant SD", presumably due to a cardiac arrythmia (CA) (6).

Dr. George X. Trimble, writing in his enjoyable Critique and Cavil in 1964, on reviewing complications of coitus (C) other than pregnancy, had not found a report from the medical literature concerning the reputed coronary attack following or during sexual intercourse (SI, I). He cited newspaper accounts of a well-known football coach found dead several

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years ago in a hotel room with a young divorcee (very much alive) in which a coronary attack as the cause of death (D) was suspected (7).

Dr. Heggtveit reported the autopsy done in 1957, of a 23-year-old soldier, a muscular 200-pounder and veteran of Korea, who died while in bed with a woman of questionable character. His heart weighed 420 grams, demonstrated severe atherosclerosis (A) and luminal stenosis but no total occlusion, and fresh and old myocardial infarctions (MI). He noted that the increased cardiac work load from the stress of C posed real problems in a population with an increasing incidence of A and leisure time. He coined the rather appropriate designation of "La Mort d'amour". (8).

Dr. Trimble subsequently told of related incidents of interest that he had received from readers (9, 10): An Illinois physician told of an instance of a "coronary attack" during SI which he had related to a "strenous psychoanalytic session" nine hours prior (the severity of the pain necessitated termination of I). A Texas physician related a case from his practice of a 56-year-old male with a past history of MI and cerebral arteriosclerosis with hemiplegia who while engaged in C, suddenly rolled over on his back, rapidly and quietly expired. A New Jersey radiologist recalled newspaper accounts of a 74-year-old senator who died in a railroad car while honeymooning with an alive and buxom "young widow". It was stated that the newspapers took the occasion to pontificate about the dangers of old men marrying lusty young women. An assistant medical examiner in Philadelphia believed that there is a significant incidence of MI associated with C but had found it difficult to elicit background information in supporting his thesis. A New Jersey physician pointed out that Holbein's "Dance of Death" implied that at least the artist may have been cognizant of the coital coronary. Montaigne alluded to the CD (1, 10).

A few other publications from the medical and other literature have addressed themselves to this subject (11, 12, 13, 14) and it is believed to account for a disportionate percentage of SD's. Rosenberg mentioned the figure of 1 percent (15). Ueno, in Japan, observed that coition D's comprised 0.6 percent of SD's (34 of 5559 cases). Eighteen of the 34 D's were due to heart disease (HD); 27 of the 34 occurred during or after extramarital I (80 percent). Cardiovascular (CV) complications ensued during extramarital transient liaison or conjugal I between an older man and a younger bride (11). Two-thirds of the D's occurred away from home, in hotels, "sweetheart's houses" and other places, although it has been surmised that probably just as many married men die at home (4). The males averaged 20 years the senior of their partners, and one-third of the victims were in a prior drunken state. It is believed that the additional stress of extramarital relations producing guilt, fear of discovery, worry about failure to perform to expectations, postprandial and post-alcoholic ingestion states and unfamiliar surroundings may augment demands and thus CV stress (4, 5).

Hellerstein and a coroner (Adelson) estimated 3 coitional SD's in 500 patients with atherosclerotic heart disease (ASHD) (14). Maimonides' statement would place the incidence a great deal higher (10). One medical examiner stated that acute coronary insufficiency (CI) resulting from C is a fact, as is sudden or immediate D during or associated with C, but the causal relationship of C to SD is still a matter of relative probabilities and controverted rather than absolute proof (4, 13). "All evidence indicates a causal relationship". A panel of experts were definitely in support of the concept (4). C becomes the proximate cause of D if the stresses and physical exertion are excessive and unusual for the particular individual at that particular time (4).

Rupp, a pathologist and medical examiner, believed it to be a definite fact, not common but yet not rare. The deceased was usually married, and D was preceded by a prior evening-out with a heavy meal and a significant amount of drinking (4). Another coroner observed this in relation to illicit sex, after rich foods (cardiac output for digestion), alcohol, and in individuals of 40-60 years. He described the story of CD transpiring in a hotel or motel; the sexual partner would call the front desk and then frequently left the scene. D usually was due to CV disease, primarily CI with or without acute MI; a number were attributed to arrythmias. Autopsy in some showed old MI's and diffuse severe coronary artery disease (CAD) (4).*

Rose, a medical examiner and forensic pathologist, was impressed by the number of SD's doing C or other sexual activity, particularly masturbation. He described a typical picture—the subject lived alone and was found with feet on the floor, body flopped back on the

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** - MI occurred during SI in 2 of 203 consecutive cases seen at the Toronto Rehabilitation Center (188).*

bed with genitals exposed, and the presence of ejacula; autopsy confirmed D from CI or intracranial hemorrhage (4).

D's have occurred in many cultures during the practice of a ligature around the neck, clutching the neck so as to compromise the carotid circulation in an attempt to accentuate and enhance sexual orgasm (strangulation) (4). Sadistic or masochistic practices have induced D during or associated with I. SD has complicated the act in the "gay world" (16), and has been noted in other situations, such as suicidal or accidental D's in carbon monoxide poisoning (4).

There may be other causes of D in relation to C: Cerebrovascular accidents (CVA's)—hemorrhage, rupture of cerebral aneurysm (Valsalva maneuver, physical activity and emotional excitement); massive pulmonary embolism (pe) (male & female)— thrombosis of leg veins with resulting pe when S is engaged in after a trip (4); June-December honeymoons (10).

Corday, while monitoring a patient with a history of precordial discomfort, found evidence of myocardial ischemia during I (12).

C is believed to have precipitated fatal ventricular fibrillations (VF) or asystole in ASHD with surprising frequency, as well as CI and D (4).

Actually, C as an unusual activity, may only aggravate or accelerate an underlying diseased CV condition—causative versus aggravative.

The author has attempted to obtain information on coitional SD in Puerto Rico. His experience has been similar to that described above. It has been generally believed that an older man here died a coitional SD secondary to the rupture of a cerebral aneurysm (autopsied). A forensic pathologist here at The Instituto De Medicina Legal in his long experience of 12,000 autopsies, has observed 2 cases of SD during SI (personal communication). These were men of ages 65 and 70 years who died during C with prostitutes in hotels or such. The cause of D was thought to be acute CI and CAD. *

Such a form of demise might not occur only in the younger segment of population (in view of the modern epidemic of disintegration of moral standards, sexual promiscuity with rising trends of venereal diseases (17, 18, 19, 20, 21) with a high prevalence of advanced CAD (22), as discovered in necropsies of soldiers dying in World Wars I and II (23, 24), the Korean—average age of 22 years; clinically silent; coronary A in 75 percent; 10 percent of these had > 70 percent narrowing of the lumen or one or more major coronary artery—and South Vietnam conflicts—less (25, 26, 27), but also in the respectable older, physically unconditioned citizen in a convention away from the tangible ties of family. There is an increased incidence of SD in age groups from 20-70 years, despite the modest physiological costs of conjugal I in older people (5, 14). Coronary heart disease (CHD) is also the chief cause of D in younger adults; half of all D's due to CHD are sudden; youth may predispose to SD in coronary attacks (22). Perhaps surprising to some, older folks certainly retain sexual interests and may present with sexual problems (28, 29, 30, 31). A coital coronary is not likely but does occur in the geriatric patient (10); 25 percent of men over the age of 70 have an active sex life (32). Peberdy reported that of individuals practicing I, 75 percent will be doing so at age 60,—about 50 percent at 70, and about 12 percent at 80 years. Penile tumescence and erections may occur in the elderly, as do irregular heart beating during REM sleep (10).

No cases of D in the female sexual partner have been cited, as the male partner has been regarded as the one at risk. Dr. Trimble surmised that if the courting habits of the male were those of the phalarope he might have a better prognosis. The phalarope is an aquatic shorebird whose unusual reproductive habits involve the female being the aggressor in courtship, while the male does the brooding, warming of eggs and rearing of the young (10). However, Massie notes that the autonomic and emotional factors in S may place a burden on the wife who is an acute or decompensated cardiac (4).

The vagrancies of love and S have also made their imprint in the lives of many famous individuals and in the footprints of history, such as Nero (33), Julius Caesar (34), Napoleon (35, 36), Henry VIII and Anne Boleyn (37). Lord Byron (38, 39), François Boucher (40), Shelley (39, 41), Keats (39, 42), Don Juan (39) and others of more recent vintage, such as movie idols, dukes and holders of high offices.

Summary

La Mort d'amour (Muerte Por Amor), sex and sudden death in relation to heart disease are reviewed.

** . The author would appreciate information on any other such deaths in Puerto Rico.*

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SINDROME ESTILOIDEO, PRESENTACION DE CASOS

Raúl E. Bertrán Escanaverino, MD, FACS

La presencia de una apófisis estiloides anormalmente elongada puede determinar síntomas cuyo origen real pasa a veces desapercibido, o ser causa de dificultades técnicas o complicaciones en el curso de la tonsilectomía.

La rápida sucesión en que tuve tres casos y la relativa rareza de la afección, me decidieron a preparar esta presentación; posteriormente pude añadir otro paciente a la estadística.

Embriológicamente la apófisis estiloides del hueso temporal procede del segundo arco branquial (cartilago de Reichert) y forma parte del aparato hioideo que es rudimentario en la especie humana (1). Anatómicamente, se proyecta del hueso temporal en su porción mastoidea, anterior y medialmente al agujero estilomastoideo por donde emerge el nervio facial. Mide unos 2.5 centímetros de longitud pero en estos casos puede elongarse hasta alcanzar 7.5 centímetros o más (2).

Presta inserción a tres músculos, el estilogloso, estilofaríngeo y estilohioideo y a dos ligamentos: estilohioideo y estilomandibular.

De acuerdo con Eagle (2) solo un cuatro por ciento de las apófisis estiloides son anormalmente elongadas, y de éstas solamente cuatro por ciento son sintomáticas. Eagle describe un síndrome que lleva su nombre, en que el paciente experimenta dolor de garganta referido al oído ipsilateral, sobre todo al tragar, sensación rasposa en la garganta, odinofagia, sensación de cuerpo extraño (espina de pescado, cerda de cepillo de dientes) otras veces un dolor sordo y contínuo en la garganta. Estos síntomas serían originados por fibrosis post-tonsilectomia y compresión del glosofaringeo, vago o facial. No obstante puede ocurrir el síndrome sin previa tonsilectomia (2, 3, 4).

Estos pacientes peregrinan de médico en médico siendo sometidos a múltiples exámenes y tratamientos sin obtener alivio y son considerados muchas veces como neuróticos. El diagnóstico se hace por la palpación digital de la amígdala palatina o fosa tonsilar (en los operados) y se confirma por estudios radiográficos.

El tratamiento es quirúrgico. Se ha recomendado por Thigpen (3) la fractura manual de la apófisis y por Loesser y Caldwell (5) el abordaje por una incisión externa en el cuello, pero la mayor parte de los autores prefieren la vía transfaringea que es la que he usado en estos casos.

Las complicaciones son raras si se usa una técnica cuidadosa, y sobre todo si no se lleva la disección hasta la base del cráneo, pues a mi juicio basta con resecar la parte saliente del hueso, unos dos centímetros. No obstante se han descrito lesiones vasculares (arterias carótidas, vena yugular interna o tri-



Fig. 1: *Hueso temporal, lado izquierdo con apófisis estiloides de tamaño normal.*

De la Sección de Otorrinolaringología del Hospital de Veteranos de San Juan, Puerto Rico y Universidad de Puerto Rico.

Trabajo presentado en la 73ra. Asamblea Anual de la Asociación Médica de Puerto Rico (20-XI-1975).



Fig. 2: *Caso No. 1. Radiografía lateral en que se observan las apófisis estiloides elongadas que casi llegan a nivel del ángulo mandibular.*



Fig. 3: *Caso No. 2. Radiografía en que se observan las apófisis estiloides anormalmente largas sobre todo en el lado izquierdo.*

butarias), parálisis facial y lesiones del glosofaringeo y del vago. También un caso de síndrome de Horner (6).

Solo mencionaré tres casos operados durante los años de 1950 a 1960 en los cuales en el curso de una tonsilectomía con anestesia local se encontró una apófisis larga que fue resecada en el mismo acto quirúrgico sin complicaciones postoperatorias; desafortunadamente no dispongo de datos más precisos.

Presentación de Casos

El primer caso de esta serie fue visto en mi oficina en 1970. Se trataba de D. N. de 65 años. Se quejaba de odinofagia desde hacía varios años con irradiación a los oídos. Tonsilectomia de pequeña, diabetes, hipertensión y obesidad. En su segunda visita y en vista de no responder al tratamiento recomendado, con anestesia tópica de Xilocaina pude palpar las prominencias de las apófisis estiloides en ambas fosas tonsilares y esto exacerbaba sus dolores habituales. Los estudios radiológicos confirmaron el diagnóstico. Al conocer su diagnóstico y explicársele las contraindicaciones relativas para la cirugía quedó tranquila. Posteriormente en 1974 fue vista de nuevo con dolor lancinante en línea media en región hioidea. Ella lo distinguía de sus síntomas anteriores. La laringoscopía reveló una lesión exofítica de base de epiglotis. La biopsia por laringoscopía directa reveló un carcinoma epidermoide. Fue tratada con cobaltoterapia y posteriormente se trasladó a New York donde ha sido seguida en el Memorial Hospital, nos dijo que había llamado mucho la atención de sus médicos su afección estiloidea y las radiografías que llevó de San Juan.

El segundo paciente es W. M. R. de 54 años visto en el Hospital de Veteranos de San Juan en 1974. Se quejaba de odinofagia del lado izquierdo con irradiación al oído desde hacía varios años. No había sido operado de las amígdalas

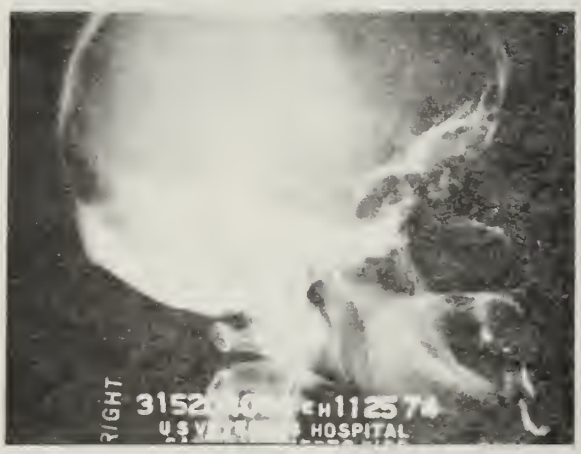


Fig. 4: *Caso No. 2. Radiografía lateral.*



Fig. 6: *Caso No. 3. La pieza operatoria.*



Fig. 5: *Caso No. 3. Concepción del artista. Después de la tonsilectomía se observa la apófisis estiloides saliente en orofaringe y el polo inferior de la amígdala aun no resecado.*

y las tenía atróficas. Fue visto hacía 3 meses por un especialista que le fracturó la apófisis manualmente sin que se aliviaran sus síntomas. Decidimos operarlo bajo anestesia general con la ayuda de nuestro residente entonces, Dr. Hernández Recio. No hubo complicaciones y el enfermo está asintomático.

La tercera paciente es A. M. G. de 35 años operada de amígdalas con anestesia local y sedación intravenosa en el Hospital Presbiteriano en 1975. Al extirpar la amígdala izquierda con el tonsilotomo de Tyding, un obstáculo óseo impidió la resección total de la amígdala quedando un resto tonsilar inferior y una apófisis estiloides saliente en faringe. Se le explicó a la enferma lo que sucedía y después de extirpar el polo inferior amigdalino se incindió la aponeurosis faríngea, se disecó la apófisis saliente seccionando el ligamento estilohioideo y cortando la parte proximal con un rongeur. No hubo complicaciones postoperatorias.

Por último y ya hecho el resumen de este trabajo, se presentó en mi oficina B. F. de 42 años con historia de crisis a repetición de dolor de garganta con irradiación al oído izquierdo. Tiene amígdalas palatinas ligeramente hipertróficas y había sido tratada principalmente con antibióticos. A la palpación de la amígdala izquierda se notó una apófisis estiloides saliente que reproducía el dolor de la enferma, el diagnóstico fue confirmado por estudios radiológicos. La paciente se tranquilizó con el diagnóstico de su afección y deseó no operarse por el momento. En estos días de nuevo me visitó pues los dolores le continuaban y desea someterse a cirugía.

Conclusión

En conclusión, queremos llamar la atención sobre

esta rara afección, relativamente poco conocida, pero no obstante fácil de diagnosticar por medio de la palpación digital y la radiología, cuyo tratamiento quirúrgico no presenta mayores dificultades.

Summary

After a brief review of the embriology and anatomy, the styloid syndrome of Eagle is studied.

1 Four cases are presented, in two of them surgery was performed without complications.

The diagnosis of an elongated styloid process is easy after palpation of the tonsil or tonsillar fossa and is corroborated after radiologic studies.

The treatment is surgical and the pharyngeal approach is recommended.

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AMA NEWS:

THREE PUERTO RICAN PHYSICIANS GAIN AMA HELP IN MEDICAID FUND

CHICAGO—Three physicians representing the Puerto Rico Medical Association met with officials of the American Medical Association in Chicago over the past weekend to seek the AMA's assistance in gaining changes in the Medicaid law as it applies to Puerto Rico.

Meeting with AMA officials were Luis A. Viñas Sorbá, M.D., President of the Puerto Rico Medical Association, Jaime A. Olmo, M.D., Immediate Past President and Emilio A. Arce, M.D., President-elect, all of Santurce. The discussions took place at the AMA's Annual National Leadership Conference at the O'Hare Marriott Hotel.

The three physicians pointed out that the Medicaid law (Section 19 of the Social Security Act) currently discriminates against Medicaid patients in Puerto Rico. A $30 million annual ceiling has been placed on Medicaid funds for Puerto Rico by Congressional mandate.

As a result, they noted, while 3.7 percent of the Medicaid population in the United States reside in Puerto Rico, the Commonwealth receives only one half of one percent of federal Medicaid funds.

The Medicaid law also discriminates against patients in Puerto Rico by denying them free choice of physician. The three medical society leaders have asked the AMA to assist them in having this restriction lifted as well.

AMA officials in Washington said they would discuss the situation with Federal officials with the objective of setting up a meeting between them and representatives of the Puerto Rico Medical Association, which represents some 2,000 physicians.

In June 1972, the House of Delegates of the AMA adopted a policy statement calling on the federal government to "apply all Federal laws relating to health and social well-being to Puerto Rico as in any other part of the nation." The government does not place an arbitrary ceiling on Medicaid funds in the various states but underwrites a percentage of program costs as determined by the economic status of the state.

FROM THE AMERICAN COLLEGE OF PHYSICIANS

INTERNAL MEDICINE SPECIALISTS TO STUDY RECENT ADVANCES AT IOWA CITY, IA., COURSE

The American College of Physicians (ACP) will sponsor a three-day postgraduate course entitled "Perspectives in Internal Medicine: a Critique of Recent Advances and Clinical Controversies" on June 7-9, 1976, in Iowa City, IA.

For information and Registration: Registrar, Postgraduate Courses, ACP, 4200 Pine Street, Philadelphia, PA 19104.

NEWS RELEASE - AMERICAN ACADEMY OF PEDIATRICS:

GENERIC PRESCRIBING FOR CHILDREN RISKY: AAP COMMITTEE.

EVANSTON, ILL. – Physicians treating children should generally prescribe specific brand-name drugs, because "the data which would allow the pediatrician to prescribe generically and expect consistent therapeutic results do not exist," according to the American Academy of Pediatrics' Committee on Drugs.

For several years, some consumers, legislators, and health administrators have advocated generic prescribing, which would allow pharmacists to substitute less expensive, generically equivalent drugs for more expensive, brand-name medications.

The Committee said that certain types of drugs – antibiotics, for example– have been tested enough so that "generic prescribing may be used with relatively more confidence."

The statement also pointed out that pharmacist's fees, overhead, the size of the prescription "and innumerable other variables may determine the cost (of the medication) to the patient more than the wholesale list price of a drug."

The Committee said it "strongly supports the use of the least expensive medication which provides effective therapy. However, the physician's duty to the patient is to prescribe reliable drugs with reproducible therapeutic effects at a given dose. Therefore, until suitable bioavailability data in children are determined and therapeutic importance recognized, the physician should continue to prescribe the products which have shown significant clinical effectiveness in his hands or in published clinical trials."

BREAST FEEDING SHOULD BE ENCOURAGED: AAP COMMITTEE

EVANSTON, ILL. – Physicians should encourage breastfeeding among mothers, the American Academy of Pediatrics'

Committee on Nutrition has recommended in the February issue of Pediatrics, the Academy's monthly scientific journal.

"However," the Committee said in a statement, "some caution is needed against issuing dire warnings to mothers who cannot or do not wish to breast-feed; normal growth and development are possible without it."

The Committee said "breast milk has not been improved on as a reference standard" for infant nutrition, and the physical contact which breast-feeding entails promotes better interaction between mother and infants – *if* the contact is desired by the mother.

The Committee noted that commercial infant formula companies have adopted policies prohibiting advertising which discouraged breast-feeding, and added:

"Physicians, nurses, and other health aides attempting pregnant and postpartum women, as well as salespersons promoting formulas, should not unconsciously encourage a negative attitude toward breast-feeding, particularly where its discontinuance may increase the risk of malnutrition. These persons are in a position to actively encourage breast-feeding."

ANUNCIO

Se alquila oficina médica, equipada, en Calle Europa Núm. 617, tercer piso, Santurce, P. R. Comparte sala de espera, cuartos de examen, records y personal para-médico con 4 médicos ya establecidos. Los interesados favor de llamar a la Sra. Sepúlveda, teléfono 724-3606.

ARTICULOS A PUBLICARSE EN LA EDICION DE JUNIO 1976

1. **Circulating Antigens, Antibodies, and Immunoglobulins in the Serum of Humans with Schistosomiasis Mansoni** – *George V. Hillyer, 1 Ph.D., Nilda Hernández-Almenas, 2, BS., Wilda B. Knight, BS, MS. 3, and Barnett Cline, 4 MD., PhD.*
2. **Cardiovascular and Phsyiological Aspects of Sex** – *Charles D. Johnson, MD.*
3. **Combined Immunosuppressive Therapy in Adult Glomerulonephritis** – *Winston Ojeda, MD., José L. Cangiano, MD, José A. Campos, MD., Rafael Ramírez González, MD., Jesús Vázquez, MD., and Osvaldo Ramírez Muxó, MD.*
4. **His Bundle Recordings in the Clinical Evaluation of Patients with Conduction Disturbances** – *Juan M. Aranda, MD, Benjamín Befeler, MD, Ralph Lazzara, MD., Nabil El Sherif, MD., and Agustín Castellanos, Jr., MD.*
5. **The Toxicology of the Phenothiazines** – *Sidney Kaye, PhD., José Rafael Rodríguez Ramos, MSc.*
6. **Metastatic Bone Tumor** – *Julio V. Rivera, MD, FACP and Andrés Acosta Otero, MD.*

LISTA DE ANUNCIANTES

1. BURROUGHS WELLCOME

   Empirin Comp. w/Codeine
   Septra

2. CIBA LAB.

   Vioform HC

3. ROCHE LAB.

   Azo-Gantanol
   Librium
   Valium

4. ROERIG & CO.
   Antivert

5. SMITH, KLINE & FRENCH

   Dyazide

6. SYNTEX LAB.

   Neo-Mull-Soy

7. UP JOHN CO.

   Medrol Dosepak

Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

Warnings: Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

Supplied: Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

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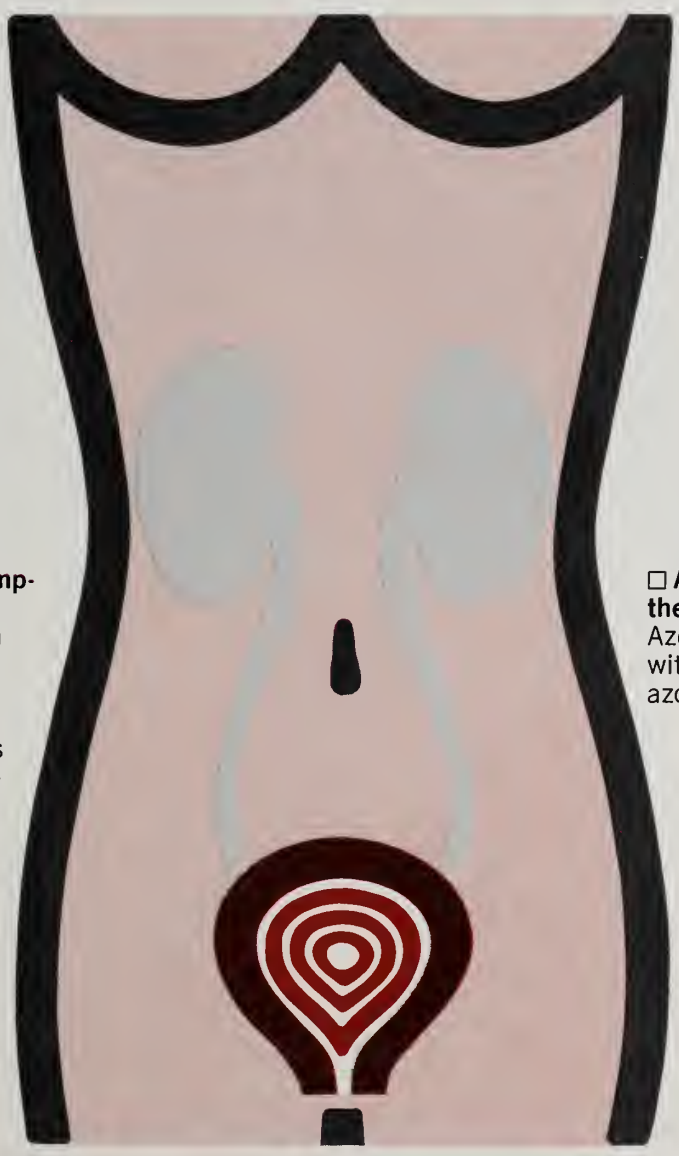
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☐ **Early relief of painful symptoms** such as burning and discomfort associated with urgency and frequency.

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FOR LONG-TERM CONTROL OF HYPERTENSION*

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Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* **Warning**
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F Co., Carolina, P.R. 00630
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The Upjohn Company, Kalamazoo, Michigan 49001

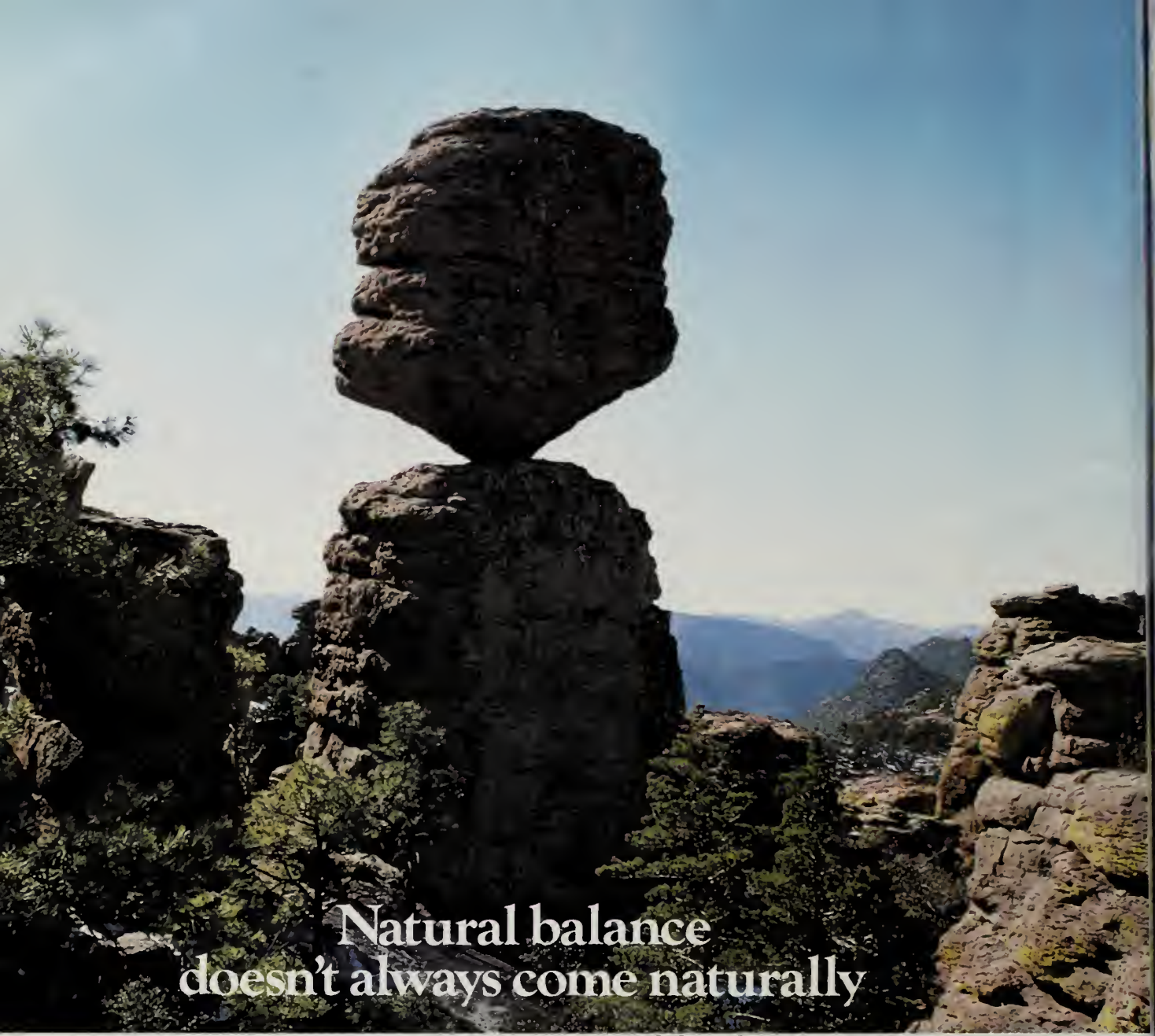
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methylprednisolone, Upjohn

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- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo.*
- Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

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A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert®/25
(meclizine HCl) 25 mg. Tablets
for vertigo*

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Ingredients per 100 grams of concentrate: water 75.2 g., sucrose 12.9 g., soy oil 6.9 g., soy protein isolate 4.0 g., potassium citrate 0.47 g., tricalcium phosphate 0.44 g., dibasic magnesium phosphate 0.11 g., lecithin 0.1 g., salt 0.06 g., calcium carrageenan 0.028 g., ascorbic acid 0.025 g., l-methionine 0.025 mg., choline chloride, ferrous sulfate, dl-alpha-tocopheryl acetate, niacinamide, zinc sulfate, manganese sulfate, d-calcium pantothenate, vitamin A palmitate, riboflavin, cupric sulfate, thiamine hydrochloride, pyridoxine hydrochloride, vitamin D_3, potassium iodide, folic acid, vitamin B_{12}.

APPROXIMATE ANALYSIS

	Undiluted	Diluted with an equal volume of water
Water	75.5%	87.8%
Protein	3.6%	1.8%
Fat	7.0%	3.5%
Carbohydrate	12.8%	6.4%
Minerals (Ash)	0.9%	0.5%
Calcium	0.17%	0.085%
Phosphorous	0.13%	0.06%
Iron	0.002%	0.001%
[illegible]	12	20



Septra DS. The same reliable formulation but doubled in tablet strength, lower in cost.

For patients with recurrent urinary tract infections

Septra DS: the same Septra efficacy in recurrent cystitis, pyelitis, and pyelonephritis due to susceptible organisms

Septra DS: the same Septra spectrum—E coli, Klebsiella-Enterobacter, P mirabilis, P vulgaris, P morganii

Septra DS: the same b.i.d. dosage schedule, but one tablet instead of two

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method *(Federal Register 37:* 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or

New Septra® DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Double Strength tablet dosage: 1 tab b.i.d.



jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **At present, data are insufficient to recommend use in infants and children under 12.**

Precautions: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

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North Carolina 27709

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e.g. the pain of
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BOLETIN

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Vol 68 Junio 1976 No.6

Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium®
(diazepam) IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

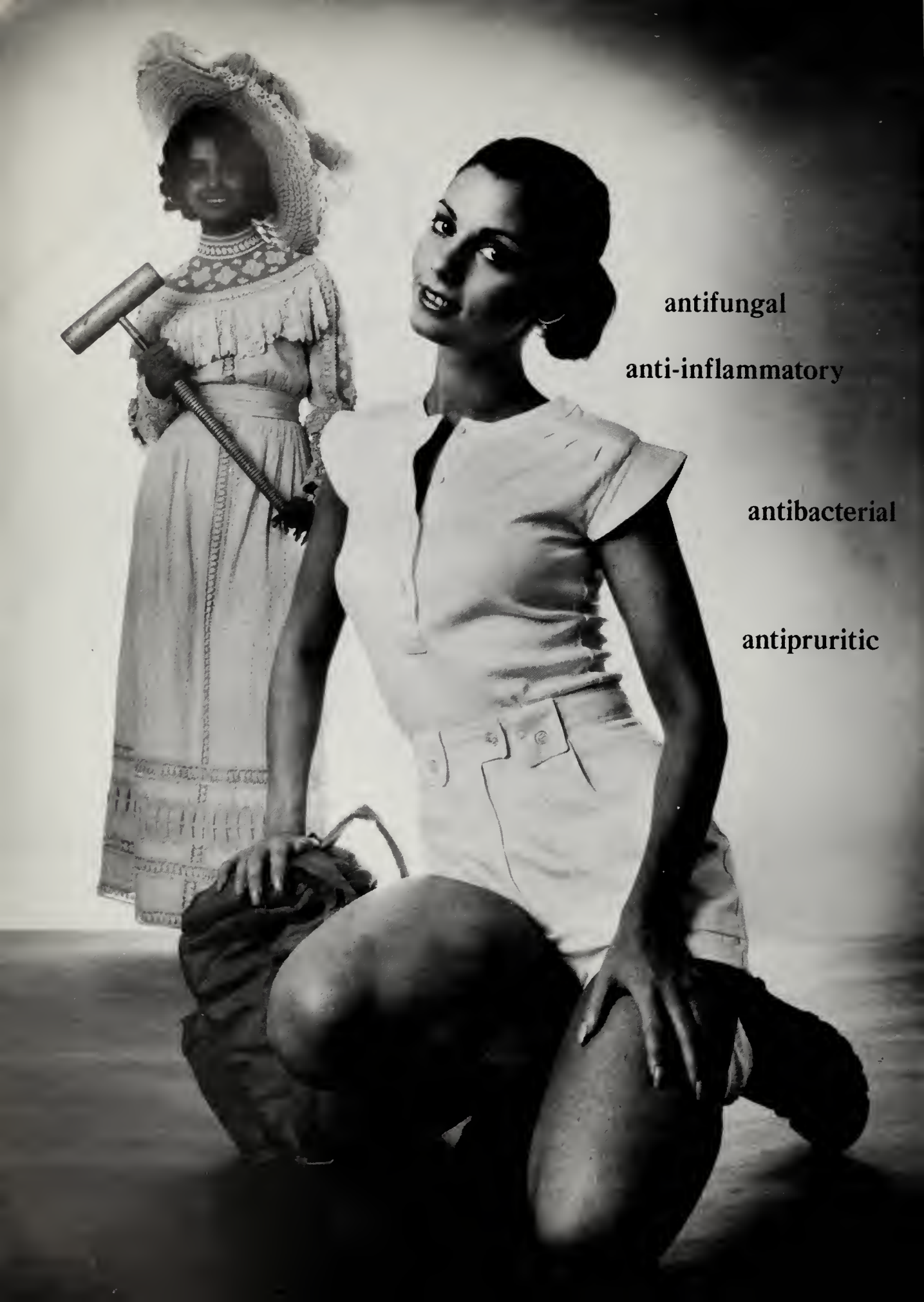
surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110


antifungal
anti-inflammatory
antibacterial
antipruritic

no place to hide...

Today's woman can't hide an unsightly dermatosis, making effective treatment a necessity.

With its unique four-way action, Vioform®-Hydrocortisone provides the kind of comprehensive therapy that many common dermatoses* require, particularly those infected with fungi or bacteria.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.
If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.
Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE
Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED
Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. *Lotion*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

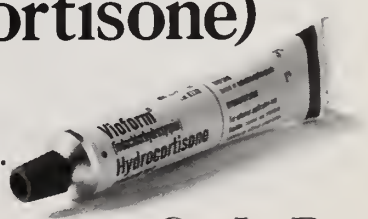
Consult complete product literature before prescribing.

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Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

the most widely prescribed form... 20 Gm Cream



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PORTADA: CONDADO BEACH HOTEL AND CONVENTION CENTER

CIRCULATING ANTIGENS, ANTIBODIES, AND IMMUNOGLOBULINS IN THE SERUM OF HUMANS WITH SCHISTOSOMIASIS MANSONI

George V. Hillyer, Ph.D.
Nilda Hernández-Almenas, BS
Wilda B. Knight, BS, MS
Barnett Cline, MD, PhD.

Experimental animals or man infected with schistosomes may develop circulating specific schistosome antigens in their serum (1-10). This has been demonstrated for mice and hamsters infected with *S. mansoni* or *S. japonicum* (1-4, 7, 8), chimpanzees infected with *S. japonicum* (6, 10), and humans infected with *S. mansoni* or *S. haematobium* (5, 9), but not for rabbits infected with *S. japonicum* (6, 10). One to three antigens have been found that cross react with adult worm homogenates, or antisera prepared against these homogenates, of the three principal species causing human schistosomiasis, indicating that the antigens may be genus-specific, but not species-specific (8, 10). Recent data suggests that at least one of these circulating antigens is produced in the gut, but not the integument, of the adult worm (11, 12). This antigen is found in the epithelial tissue of the gut and at the border of these cells with the lumen. Diastase-fast, PAS-positive staining in the antigen-containing areas of the gut suggest this antigen is a polysaccharide (12).

The presence of circulating antigen is of interest because of its reported relationship to worm burden early in infection of mice and hamsters with *S. mansoni* (1, 2, 7) and because of its possible role in immune complex nephropathy associated with *S. mansoni* (4, 6, 9, 10, 13).

This study represents a preliminary effort to determine whether there is an association between the presence of circulating antigens and the level of egg excretion in humans. We compare the presence or absence of circulating schistosome antigens or antischistosome precipitins in humans with varying levels of excretion of *S. mansoni* eggs and also present data on serum immunoglobulin levels for IgG, IgM, IgA, and IgD.

From the Department of Biology, University of Puerto Rico, Río Piedras, P. R. 00931, and San Juan Laboratories, Bureau of Laboratories, Center for Disease Control, Public Health Service, US Department of Health, Education and Welfare, G. P. O. Box 4532, San Juan, P. R. 00936.

Materials and Methods

Twenty-six human sera were selected from approximately 776 samples collected during November 1971 as part of a prospective study of schistosomiasis in a rural community (13). The community, near Las Piedras in eastern Puerto Rico, had 1,035 inhabitants, of whom approximately 40 percent were infected with *S. mansoni*. The criteria for selecting sera were that (1) parasitologic results were available from the same individual, (2) the specimens included a broad spectrum of intensity of infection as reflected by *S. mansoni* eggs counts, (3) both sexes and a wide range of ages were represented, and (4) none of the sera were from persons who had received antischistosomal drug therapy within 10 years.

S. mansoni eggs counted by a single modified formalin-ether concentration technique which examines one gram of feces (W. B. Knight, manuscript in preparation). This technique is sensitive compared to other commonly employed fecal examination techniques (B. L. Cline, unpublished observations). The 26 individuals studied, ordered on the basis of *S. mansoni* eggs/ gram of feces, are listed with age and sex (Table I). Sera were obtained from five Puerto Rican university students who had no helminth eggs in one stool examination and both negative skin and circumoval precipitin tests to *S. mansoni*. These served as "normal" controls.

Soluble cercarial, adult worm, and egg extracts of *S. mansoni* were prepared by techniques previously reported (14). Each extract was used with Freund's adjuvant to hyperimmunize rabbits, and the antisera thus produced were used to detect the presence of circulating schistosome antigens in each human serum. The antigenic extracts were also used to test for precipitating antibody (15). The tests for circulating antigen or precipitating antibody were done in microslides containing 1 percent agarose (14). Commercial immunoplates were used to quantitate serum immunoglobulins (Ig). Immunoplates from Kallestad Laboratories were used to measure IgG, IgM, and IgA. Antihuman IgD immunoplates from

TABLE I
RESULTS OF IMMUNODIFFUSION TESTS FOR SCHISTOSOMAL ANTIGEN AND ANTIBODY IN SERA FROM 26 PUERTO RICANS WITH SCHISTOSOMIASIS MANSONI

Serum No.	Eggs/gram	Age	Sex	Number of Precipitin Lines To: CE[a]	Anti-CE	WWE[b]	Anti WWE	EE[c]	Anti EE
1	2483	13	M	1	1	2	1	0	0
2	1610	23	M	2	0	2	0	2	0
3	1176	25	F	0	0	0	0	1	0
4	608	27	F	1	1	1	1	0	0
5	568	35	M	2	0	2	0	1	0
6	432	35	F	0	0	0	0	0	0
7	410	11	M	0	0	0	0	1	0
8	360	30	M	1	0	1	0	1	0
9	330	26	M	1	0	1	0	0	0
10	284	38	M	1	1	2	1	1	0
11	250	30	F	0	0	0	0	1	0
12	228	10	F	0	1	0	0	1	0
13	199	25	F	1	1	2	1	2	0
14	187	8	M	1	1	0	0	0	0
15	182	15	M	0	0	0	0	2	0
16	88	40	M	2	0	2	0	2	0
17	71	12	F	0	0	0	1	1	0
18	32	18	F	1	0	0	0	0	0
19	15	35	F	0	0	0	0	0	0
20	11	17	M	1	0	5	1	2	1
21	7	13	M	0	0	0	1	0	0
22	7	20	F	0	0	0	0	2	0
23	4	24	F	0	0	0	0	2	0
24	2	50	F	0	0	0	0	0	0
25	2	16	M	0	0	0	0	1	0
26	1	38	F	0	0	0	2	1	0

a. Cercarial extract
b. Whole worm extract
c. Egg extract

Hyland Laboratories * were used to measure IgD.

Results and Discussion

I. Circulating schistosome antigens.

Results of the immunodiffusion tests for circulating schistosome antigens and precipitating antibodies were determined for each serum specimen (Table I). Six of the serum samples had cercarial antigens, eight had adult worm antigens, and one had egg antigen. The number of circulating antigens, as indicated by the number or precipitin lines, varied between 0 and 2 for each life cycle stage. Human serum from uninfected controls did not have circulating schistosome antigens. Some sera from humans with schistosomiasis mansoni had circulating antigens to one life cycle stage but

** - Use of trade names is for identification only and does not constitute endorsement by the Public Health Service or by the U. S. Department of Health, Education, and Welfare.*

TABLE II
IMMUNOGLOBULIN LEVELS IN SERA FROM 26 PUERTO RICANS WITH SCHISTOSOMIASIS MANSONI

Serum No.	Immunoglobulin Concentration (mgm/100 ml) G	M	A	D
1	1850	140	260	3.52
2	3800	300	380	0
3	1580	120	217	3.9
4	1550	175	280	8.8
5	1460	110	380	3.15
6	1550	175	260	4.5
7	1480	93	290	3.2
8	1480	51	217	6.0
9	2000	94	200	10.
10	1940	170	355	3.7
11	2000	66	325	5.12
12	1750	110	172	2.4
13	1600	300	340	0
14	2100	85	129	3.1
15	3600	72	110	2.75
16	1280	144	120	0
17	2000	110	102	3.7
18	1150	144	186	0
19	1650	61	N.D.	0
20	1260	160	200	3.2
21	1480	144	268	0
22	1480	94	186	2.75
23	1080	40	186	0
24	1300	61	96	3.3
25	2000	110	129	0
26	1480	86	N.D.	3.15

not to others. Thus the results suggest that, in addition to circulating adult worm antigens, other stage-specific schistosome antigens are present in the circulation. The serum of a patient with schistosomiasis and glomerulonephritis was found to contain a circulating schistosome *egg* antigen, but not an adult worm or cercarial antigen (16). This is further evidence that stage-specific circulating antigens may be found.

No clear relationship was apparent between the number of eggs excreted in the feces of the individual and the presence or absence of circulating antigens. This is of interest since Cheever has demonstrated in humans with schistosomiasis mansoni a direct relationship between the number of eggs per gram of feces and worm pairs recovered (17). In addition, several investigations, using quantitative techniques, have demonstrated in mice and hamsters a direct relationship between circulating schistosome antigen and worm burdens during early patency (1, 2, 7). In a qualitative study with chimpanzees infected with *S. japonicum*, larger numbers of circulating antigens were found during early patency than later in the infection (6, 10). In human populations where duration of infection is difficult to determine, the apparent lack of correlation between circulating antigen and worm burden may be due to the variable duration

of infection in the study population. This study shows that in addition to circulating adult worm antigens, cercarial and egg antigens are also found in the serum of infected persons.

II. Circulating chistosome antibodies.

The number of precipitins to cercarial (CE), whole worm (WWE), and egg (EE) extracts in each serum are summarized (Table I). No precipitin lines were observed with normal sera. Of the sera from the infected cases 10 (38 percent) reacted to adult worm extract of which 3 had one precipitin, 6 had 2 precipitins, and 1 had 5 precipitins. Twelve sera (46 percent) reacted with cercarial extract. Of these, 9 had 1 precipitin, and 3 had 2 precipitins. Seventeen sera (65 percent) reacted to egg extract of which 10 had 1 precipitin and 7 had 2 precipitins. More significant was the finding that 23 of the 26 sera (88 percent) did react with at least one antigenic extract. Neither the number of precipitate bands nor the intensity of them was dependent upon the number of eggs per gram of feces.

A previous serologic study of humans with schistosomiasis mansoni showed that sera from chronic cases had diminished quantitative as well as qualitative precipitin responses to schistosome antigens when compared to sera from acute cases (15). However, all of the sera reacted with at least *one* antigenic extract. In another report, 67 percent of 15 human sera from individuals infected with *S. mansoni* reacted with adult worm antigen or eggs, or both (4). In both studies, as in this one, sera reacted most frequently with egg extract, and the adult worm extract was the poorest antigen. Other workers have reported poor results in detecting chronic cases of human schistosomiasis by double immunodiffusion utilizing adult worm extracts (18). A possible reason for the difference in results may be that the extract found optimal for use in this study was fourfold more concentrated than that used in the previous study. As we have demonstrated herein, use of three different antigenic extracts increases the probability or reactivity with at least one extract.

III.Immunoglobulin levels.

The results on serum immunoglobulin levels are summarized in Table II. The serum numbers of Table II correspond to those of Table I. The average IgG levels for the cases of schistosomiasis mansoni was 1,700 mgm/100 ml ranging from 1,050 to 3,800. The five normal human sera averaged 1,080 mgm/100 ml with a range of 840 to 1,500. IgM levels were also higher in the infected group averaging 127 mgm/100 ml as compared to 109 for the normal group. IgA levels were similar in the infected and control groups having an average of 229 and 219 mgm/100 ml respectively. IgD levels were low in both groups averaging 2.6 and 3.4 for the infected and normal group, respectively.

The serum IgG, M, and A levels are remarkably similar to those reported in a previous study of Puerto Ricans with schistosomiasis mansoni (15). The literature on this subject has been reviewed previously (4). Serum IgD levels have not, to our knowledge, been reported for humans with schistosomiasis. In this study population, they appear to be within the normal range.

Summary

Many humans excreting varying levels of *Schistosoma mansoni* eggs in their feces have circulating parasite antigens in their serum. In addition to circulating adult worm antigens, additional antigens similar to those found in cercariae and eggs are observed. With respect to circulating precipitating antibodies, 88 percent of the sera from infected individuals reacted with at least one antigenic extract. Those that were non reactive were from older individuals. Serum IgG and IgM were elevated in the infected individuals, whereas serum IgA and IgD were within normal values.

Resumen

Humanos con esquistosomiasis mansoni, con cantidades variables de huevos en las heces, tienen en su sangre antígenos circulantes del parásito. Estos antígenos reaccionan con antisueros preparados con gusanos, cercarias, o huevos de *S. mansoni.* Estos individuos también poseen anticuerpos circulantes contra el parásito. Cuando los sueros se prueban contra antígenos de gusano adulto, cercarias y huevos, un 88 por ciento de ellos tienen una prueba positiva. Los que no reaccionaron eran de casos mayores de 30 años de edad. Se determinaron, además, las concentraciones de inmunoglobulinas (Ig) en estos individuos. IgG y IgM estaban elevados en los casos con esquistosomiasis; IgG y IgD estaban en concentraciones normales.

Acknowledgments

The serum Ig quantitation was done with the technical

assistance of Rosa Lluberes (General Medical Research Laboratory, Veterans Administration Center, San Juan, Puerto Rico). The fecal specimens were collected by Mr. Luis Berríos Durán (San Juan Laboratories). These studies were supported in part by NIH Grant No. RR-8102.

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CARDIOVASCULAR AND PHYSIOLOGICAL ASPECTS OF SEX

Charles D. Johnson, MD

Physiological and Hemodynamic Aspects

Klumbies and Kleinsorge in 1930 may have been the first to publish medically on circulatory aspects of sexology (43). A questionnaire study on SI in American married couples was made in 1931 by Dickinson and Beam (44). Boas and Goldschmidt in 1932 on studying sexual physiology found an average HR during sexual intercourse (SI) of 149 beats per minute, which was more than the rate found on standing (91), walking (118) or dancing (131). An increase in cardiac output (CO) was inferred. The emotions in addition to the exercise were considered causative factors (45). Kinsey published his rather shocking study in 1948 (46). Further German studies were reported in 1950 (47). In more recent years scientific studies have elucidated the physiological, electrocardiographic and hemodynamic changes transpiring in normal individuals and in subjects with ASHD during sexual activity. In 1956, Bartlett demonstrated the physiological stress on the CV and pulmonary systems during C in the human (48, 49). There was a marked increase in HR accompanying orgasm in both the male and female; also, a marked increase in the respiratory rate (RR) (60/min.) and minute volume (30-50 L-normal about 7 L) occurred during erotic arousal and orgasm in many of the tests. The data suggested that hyperventilation was present during erotic arousal and particularly during orgasm. Muscle rigidity was associated with the latter. The magnitude of the HR during sexual response, especially during orgasm, was comparable to that produced by strenous forms of isotonic exercise.

So C must be regarded as work (10) and can be potentially harmful to the CV system. Masters and Johnson observed rates during orgasm of 110-180/min in both males and females while increments in BP in males ranged from $\frac{40\text{-}80}{20\text{-}50}$, and in females from $\frac{30\text{-}80}{20\text{-}40}$ mmHg (5, 50). HR, ventilation and the response of organs such as breast, genitalia and skin during phases of the act were studied. Studies from the German and American literature have documented marked, generally parallel rises in HR, RR, systolic and diastolic BP's during all phases of the sexual act, the pulse during orgasm rising as high as 170/min or 100 beats over the resting level within 1 minute and returning to normal equally rapid (51). RR's were sometimes over 60/min and BP sometimes as high as $\frac{250}{120}$ mmHg.

The phases of the sexual act have been divided into four: 1. Excitement or erotic arousal during foreplay, 2. Intromission-plateau, 3. Orgasm, and 4. Resolution (47, 50, 52).

HR, BP and minute ventilation augment in a progressive fashion during erotic arousal and intromission, rapidly peak at ejaculation and orgasm and decline to control levels as rapidly during resolution (14). The HR and BP responses may be partly emotional (excitement) and partially due to B-sympathetic activity as they have been modified downward by B-blockade with propranolol (53, 54). Cardiac symptoms of a fast HR and AP are most likely to manifest in the resolution phase (5, 14). The increments in HR occur irrespective of the technique of stimulation (50). C and sexual arousal may affect other body parameters (5, 53, 54). Testosterone levels are augmented in males, and may possibly be a factor in the production of CAD. Oxytocin is released and may cause the milk ejection of sexual arousal of lactating females. The posterior pituitary may be involved in post-C antidiuresis. There were no significant changes in post-C blood levels of serotonin or prostoglandins, but non-esterified free fatty acids rose during sexual arousal (10). Average systolic BP has been found to increase slightly (+ 14 mmHg) in male sophomore medical students watching a movie of a nude female, as have urinary catecholamines (epinephrine and norepinephrine)—up to 66 percent—in males watching a pornographic movie.

Some believe that the respiratory alkalosis from hyperventilation may produce sensory phenemona, augment systemic vascular resistance (SVR) and aggravate ischemia in patients with poor circulation by decreasing the amount and rate of oxygen (O_2) release from he-

moglobin-Bohr effect on Hb-O_2 dissociation curve (5).

Nasal stuffiness and sneezing are known to occur during sexual excitement; an increase in nasal temperature and nasal blood flow were found experimentally (10).

Dr. H. K. Hellerstein has been noteworthy in these most recent scientific studies and advancements in learning, and the majority of the following information is derived from his ingenious work. Data has been obtained from historical information, examination, questionnaire survey, electrocardiography, stress testing by bicycle ergometry and by Holter tape monitoring (Sexercise Test) on subjects, and married couples in the natural environment of their own bedrooms.

It has been emphasized that the studies showing the "tremendons jolt" of physiological changes (studies described above)—marked tachycardia, hypertension (H) and hyperventilation observed in young "volunteers"—should be sharply distinguished from those noted by Dr. Hellerstein in middle-aged married males (to be described below) engaging in S in their own home with their wives of 25 years (5, 14, 52). The "volunteers" in general were young married couples or older, had marital or sexual problems, were unmarried, divorced, were prostitutes or were "suspect" just for volunteering; and the subjects were studied under direct, laboratory and unnatural conditions.

In studies of postcoronary patients (ASHD) and control coronary prone subjects, Dr. Hellerstein confirmed the impression that sexual activity declined with age in normals, and decreased further in 58 percent of patients (4 times weekly at age 25 to 2x weekly just prior to the MI) (14). It depended upon prior sexual behavior, socioeconomic status, drug intake, previous and present CV function, response to therapy (medical, physical training), and associated diseases. C was resumed on an average of 13.7 weeks after an MI. 42 percent of this group (48) of males, 3 months or more post MI suffered CV symptoms during or immediately after SI. The frequency of orgasms per week decreased from 2.1 to 1.6 in these patients. AP developed in 21 percent, and was favorably influenced by systematic physical reconditioning. Only 27 percent of symptomatic subjects were required to discontinue sexual activity, and symptoms of CI infrequently influenced return to such (14). The average time to maximal HR (MHR) after retiring to bed was 16 minutes (10-30"). In 74 percent of cases an average of < 10 minutes elapsed from the beginning of phase 2 till the husband's ejaculation. In the questionnaire study of 1931 the duration of I was likewise short (44). In the studies carried-out 3 months post-MI, the MHR response averaged 117/min (range of 107-130) for 10-15 seconds (sec), and 85-102 beats/min one and two minutes before and after maximum. Maximum oxygen consumption (VO_2 max) was 11.9 (45 percent) (average HR) and 16 ml/kg/min (60 percent) (MHR). The equivalent O_2 cost of maximal activity during I approximated 6 calories (C) per minute, 5 Mets (M), for less than 30 secs, and about 4.5 C per minute, 3.7M, during the pre-and postorgasmic periods. Electrocardiographic changes consisted of tachycardia, ectopic beats (28 percent) and ST segment depression, the significance of the latter have been questioned in view that distortions in the recording system and positional activity may affect them (13). These energy levels and demands on the heart are equal to walking briskly on the street, climbing one or two flights of stairs, performing ordinary tasks in many occupations or a Master's 2-Step Test (22.3 ml O_2/kg—6.8 M) (14).

Both normal subjects and middle-aged, middle-class, long-married (26 years) patients with ASHD engaged in SI approximately twice weekly, the duration of the act totaling no more than 0.3 percent of living time. The duration of CV stress was short, about 4-6 minutes. This low ebb sexual activity picture pertained also to healthy married couples of the typical hypokinetic, physically unconditioned middle-age male, in which comparable CV stresses were encountered frequently during the performance of low energy requiring occupations, arguments or driving in traffic (14, 52). The personality profiles of these ASHD patients were abnormal. Prolonged sensous sexual activities appeared to be an exception in both groups.

Problems

It is well known that people, including wives, are inhibited in expressing sexual feelings and concerns, and physicians have likewise been hesitant in initiating such discussions (55). Concerns of sexual adequacy, permissible types of sexual activity, libido and fear of D with I (men and their wives) are prevalent in patients recovering from MI's, even after medical reassurance (56). One psychiatrist observed that sex problems were more common in coronary patients (57). Acute emotional stress was noted in 37 percent of post-MI patients, and 49 percent of patients demonstrated

sexual problems such as loss of libido, feelings of premature aging and growing old, decreased potency, ideas of loss of manhood, and premature ejaculation. Decreased interest, phobia or perhaps "hypersexuality" (58), or complete cessation of C (59) may prevail. The lowered frequency of S may be quite remarkable, and is sometimes on the basis of the spouse's decision rather than from symptoms or on a physician's advice. Impotence has developed rarely, up to 30 percent of such patients, sometimes permanently (14, 60, 61). In 40 survivors of acute MI, 22 percent recalled lowered libido as a pre-infarction symptom (62). Beliefs exist that even mild exertions kill, SI should never be attempted again, and that repeat heart attacks may occur at orgasm (13-Hackett in Ref. 13). Six of 10 cardiac arrest patients demonstrated a decrease or discontinuation of sexual activity, and the wives were advised to "take it easy" (63). So, misinformation and fear often reign in controlling sexual activity. And all this in the face of the fact that the male coronary patients are more flirtations and seductive, and the post-MI male, beginning at 3-8 weeks, has S on his mind (13, 64)—an added stress?

Masters and Jaffe found that only 8.7 percent of coronary occlusions or CI occurred during moderate activity (which included C). CI is more common and is associated with a precipitating factor in 1/3-1/2 of cases (65). Green stated that worry over a coronary occlusion only during C alone seemed unjustified, although CI is a possibility but justifying no greater concern than should most routine activities (13).

Besides the rare documentation of SD associated with C, is the much broader scoped problem of sexual activity and behavior in individuals with the widespread epidemic of HD, particularly that of ASHD. Here, important connotations are evident in the mass of populace with silent CAD, AP, and in the management and rehabilitation of the post-MI patient.

In the past there has been a scarity in the medical literature of information, facts and data on matters of S and sexual rehabilitation. Hellerstein and Friedman noted in 1969 that in a review of 33 cardiology textbooks less than 1000 words referred to sexual activity and the heart (52). The majority of publications have been isolated reports, experiences and impressions (13).

Also, the medical training of physicians in the past, both at the medical school and post graduate levels, has been noteworthily limited or completely devoid of instruction in sexuality. Accurate lay knowledge and often that possessed by physicians too, has been essentially nil, as feelings, beliefs and actions have their basis upon hearsay, folklore, lockerroom talk, testimonials and fear.

Dr. William Masters has pointed out that "physicians probably know no more and no less about the subject than do other college graduates, and share the common misconception, taboes, and fallacies of their nonmedical confreres". Davis, in Eros and Thanatos, decried such a state of affairs in the education of physicians in sexuality and D (66).

The family doctor in one study was listed by 60 percent of respondents as a preferred source of sex information, but only 5 percent said that the doctor had actually provided them with such. The AMA House of Delegates (32) noted that people identify doctors as "a primary source of sexual information and counseling", "but physicians are often not prepared to meet this responsibility". 44 percent of 112 patients reporting sexual discussion, believed such discussion was helpful (CV patients comprised the second largest group) (67).

It is distressingly true that often the post-MI patient is not given specific medical advice or a prescription on physical activity (other than to tell him or her "to take it easy"), psychological and work rehabilitation, much less medical information and advice on sexual matters, which assume so important a role in the psychological and emotional rehabilitation of the cardiac patient.

A study in 1964 of men who had suffered a MI 1-9 years prior, seen in a cardiac work evaluation unit (two-thirds less that 50 years of age) revealed that two-thirds had received no advice regarding sexual matters, while one-third had been given vague, nonspecific advice. A few suffered anginal pain during I. There was an average period of 3 months from the MI incident until SI. Only one-third resumed a normal pattern of sexual activity, while in two-thirds a marked and lasting decline in frequency occurred; 10 percent became permanently impotent. The patients set their own behavior, based on fear and misinformation (61).

It has been recommended but only recently has it received any recognition, that members of the medical profession offer advice and information on aspects of S, because of its importance in the total rehabilitation of the heart patient, and since D's do occur. It has been stated that "unfortunately, reticence, lack of information, lack of time, lack of training in how to discuss such matters, some personal bias and a surprising lack of life experience hamper some members of the medical profession in so doing (14, 51).

Apparently notable exceptions do exist. From a Hellerstein questionnaire, 94 percent of physicians said that they had counseled on S, using clinical judgment and tolerance of daily activities or functional capacity by standard exercise testing (18 percent). (14). And one Texas cardiologist reported that 90 percent of his colleagues counseled patients on S (68). However, physicians' advice in respect to S in cardiac patients has been one of notable conservatism (59). 83 percent suggested limited activity, 5 percent suggested abstinence for 2 weeks to 3 months (average 6-8 weeks), and 13 percent advised unlimited activity. 70 percent believed that SD is a realistic possibility and 31 percent would advise patients of such.

The AMA has urged medical schools and organizations to offer formal instruction to physicians on human sexuality at undergraduate, graduate and continuing medical education levels. Today the situation has changed and nearly all US medical schools are teaching students in respect to human sexual behavior and sexual dysfunction. Postgraduate educational courses are now available and there are courses for physicians who want to specialize, or become sex counselors or therapists (32).

Berkman noted the inadequacy in sexual and psychological counseling and discussed the role of rehabilitation. It was believed that physicians and hospital staffs should receive sex education to promote better counseling to patients (69).

Summary

Some cardiovascular and physiological aspects and problems in sexuality are reviewed.

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COMBINED IMMUNOSUPPRESSIVE THERAPY IN ADULT GLOMERULONEPHRITIS

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Despite major advances in immunology the precise pathogenetic mechanisms involved in the genesis of glomerulonephritis, remain unsolved. However, the pathological lesion is generally believed to be the result of an immunologic response (1).

This lack of knowledge has precluded the development of satisfactory treatment for adult glomerulonephritis. Likewise, prevention of the disease is not feasible without exact knowledge of the basic mechanisms and symptomatic treatment merely alters some of the manifestations of the disease rather than the basic pathological abnormality. The specific treatment may be divided into two general categories: (a) anti-inflamatory or (b) inmunosuppressive. Steroids are an example of the former and azathioprine and cyclophosphamide of the latter. The long term results from steroid therapy in adult glomerulonephritis associated with nephrotic syndrome is disappointing and uncertain (2). This, together with the encouraging reports of the use of cyclophosphamide (3) in children with nephrotic syndrome, and the paucity of published data in adults has prompted us to treat a group of adult patients with glomerulonephritis with a combination of steroids, azathioprine and cyclophosphamide.

Materials and Methods

The patients were incorporated in this study after the diagnosis of glomerulonephritis was established by clinical and histological criteria. Those patients with systemic lupus erythematosus, diabetes mellitus, amyloidosis, malignancy, renal vein thrombosis, known exposure to heavy metals or acute glomerulonephritis, were excluded from the study. All patients had either severe proteinuria and/or a reduction in glomerular filtration rate as measured by creatinine clearance. Percutaneous kidney biopsies were performed in all patients, with the aid of an image amplifier and processed for light, electron microscopy and immunofluorescent studies. According to the histological changes, the patients were classified into 3 main types of lesions, membranous, proliferative and mixed (membrano-proliferative).

The renal tissue was processed with buffered formalin and stained with hematoxylineosin; Masson trichrome, periodic acid Schiff (PAS) and PAS methenamine silver stains. Electron microscopy studies and immunofluorescent studies using anti IgG, IgA, IgM and B_1C were also performed.

After fulfilling clinical and histologic criteria an informed consent was secured from each patient. They were advised of the nature of the study, attendant risks and side effects, expectation of treatment and of the follow-up requirements. Nineteen patients, 16 males and 3 females entered the study. Their ages ranged from 22 to 58 years (mean 41). Twelve patients showed membranoproliferative glomerulonephritis, 4 showed purely membranous and 3 proliferative glomerulonephritis. Immunofluorescent studies were accomplished in 7 patients who showed deposition of IgG and complement (B_1C). IgM deposition was observed in 4 patients. Prednisone 40 to 60 gms every other day, cyclophosphamide 50-100 mgs daily and azathioprine 50-100 mgs daily were given to all patients for periods of 8 to 24 months. The following studies were performed before treatment and at monthly intervals; urinalysis, 24 hour creatinine clearance, 24 hr urinary protein, total protein, serum albumin, serum globulin, serum cholesterol and serum complement. Complete blood and platelet counts were performed every two weeks. WBC count was maintained over $3{,}000/mm^3$ during the duration of the study. The creatinine clearance was performed in the Renal Laboratory, and all other laboratory tests were performed by standard techniques in the Clinical Laboratory of the San Juan Veterans Administration Hospital.

The clinical criteria of response was divided into excellent, good or poor based on proteinuria and glomerular filtration rate (Table I).

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TABLE I
CLINICAL CRITERIA OF RESPONSE

Excellent	-	complete clinical remission with proteinuria less than 300 mg per 24 hour and normal creatinine clearance (100 cc/min/1.73 m^2).
Good	-	a) proteinuria less than 1.25 gm per day. b) a 50 percent or more drop in proteinuria. c) a less than 15 percent reduction in creatinine clearance.
Poor	-	no significant improvement in proteinuria or creatinine clearance by the above criteria.

TABLE II

				Before Treatment		*After Treatment*		
Case No.	Sex	Age	Kidney * Pathology	Urine Protein Gms/day	Creatinine Clearance	Urine Protein Gms/day	Creatinine Clearance	Duration of Treatment Months
1	M	40	MP	0.7	61	0.9	60	15
2	F	39	MP	0.18	84	0.1	97	19
3	M	22	P	1.9	76	0.8	72	16
4	M	40	MP	2.1	89	1.7	92	14
5	M	23	MP	16.3	63	13.2	70	12
6	M	40	MP	13.5	93	4	99	17
7	M	26	MP	4	86	3.6	44	19
8	M	36	MP	3.4	84	2.7	79	17
9	M	35	MP	3.9	109	3	98	17
10	M	51	MP	1.6	56	0.8	65	12
11	M	32	P	7.5	25	6.5	13	22
12	M	32	P	6	52	3.8	38	29
13	M	49	M	11	106	5.4	127	17

* *M - mebranous*
P - proliferative
MP - membranoproliferative

Results

None of the 19 patients had an excellent clinical response, 6 had a good response and 13 had a poor response (Tables II and III). Of the 6 patients with a good clinical response, 4 had membranoproliferative glomerulonephritis and 2 had a purely membranous glomerulonephritis. Improvement in the histological findings was demonstrated at the end of the treatment period, however, immunofluorescent findings remained unchanged. Patients with a poor clinical response did not show any histological improvement, 9 had membranoproliferative, 3 proliferative and 1 membranous glomerulonephritis. Only one patient became worse

TABLE III

Case No.	Sex	Age	Kidney * Pathology	Before Treatment Urine Protein Gms/day	Before Treatment Creatinine Clearance	After Treatment Urine Protein Gms/day	After Treatment Creatinine Clearance	of Treatment Months
14	M	40	MP	4.1	123	2.4	106	17
15	M	57	M	5.4	37	1.2	45	27
16	F	58	M	8.0	68	0.1	71	19
17	F	51	MP	3.1	67	0.9	73	11
18	M	38	MP	0.4	57	1.2	90	14
19	M	43	M	5.3	70	1.0	115	18

** - M - membranous*
MP - membranoproliferative

during the study period and required chronic hemodialysis treatment. All patients with good clinical response had no deterioration of renal function or increased protein excretion in follow up of several months after discontinuation of the medication.

Serum complement levels were repeatedly low in three patients (2 with poor response, I with good response). At the end of the treatment period the complement levels increased to normal values in spite of their therapeutic response.

No serious toxic reactions were encountered using the combination of the three medications. All medications were discontinued whenever the WBC count reached 3,000 or less, and reinstated as soon as the count increased.

There were no episodes of overt infection, hemorrhagic cystitis or hepatitis. A few patients described minimal to moderate loss of hair which did not require discontinuation of medication.

Discussion

It is generally accepted that nephrotic patients with normal or minimal changes in biopsy specimens will benefit from steroid therapy (4, 5). Similarly, patients with highly selective proteinuria, consisting mainly of albumin, are more likely to benefit from corticosteroids. In contrast, adult patients with glomerular disease have demonstrated no benefit from steroid therapy in proliferative, membranous or membranoproliferative glomerular lesions (6).

Immunosuppressive agents have been used by several investigators but the results have been conflicting. Abramowicz et al (7) demonstrated no significant benefit from the administration of azathioprine in 49 children with steroid resistant nephrotic syndrome. In contrast, Barrat and Soothill (3) showed that cyclophosphamide reduced the frequency of relapses in 30 children with recurrent nephrotic syndrome.

In adults the use of immunosuppressive agents alone or in combination with steroids has also been advocated. A large, carefully controlled study by the Medical Research Council of Great Britain (8) demonstrated that combined therapy with azathioprine and corticosteroids offered nothing other than adverse effects to adult patients with proliferative glomerulonephritis.

A synergistic effect in the suppression of immune responses has been observed with combinations of biochemically related antimetabolites (9). These observations have led to the use of triple-drug therapy instead of double-drug therapy. Based on this assumption, Mukherjee (10) reported complete remission of proteinuria in 10 of 12 patients with a combination of prednisone, azathioprine and cyclophosphamide. In this study the dosage of drugs used and tests of renal function, namely, glomerular filtration rate measurements, were not reported.

Our results with triple drug therapy in 19 patients with glomerulonephritis are not as encouraging. No excellent response according to our clinical criteria for improvement was observed. In contrast to other studies the large majority of these patients had membranoproliferative lesions. No correlation of response to complement levels was observed. In conclusion, triple drug therapy for periods up to 29 months is not completely effective in reversing the abnormalities associated with membranous, proliferative and membrano proliferative glomerulonephritis. In our hands immunosuppressive therapy of glomerulonephritis seems to be very discouraging and other forms of therapy should be explored.

Summary

Nineteen adult patients with membranous, membranoproliferative and proliferative glomerulonephritis with severe proteinuria and/or reduction in glomerular filtration rate were treated with a combination of prednisone, cyclophosphamide and azathioprine for periods of 8 to 29 months. None of the patients had an excellent response; 6 had a good response and 13 had a poor response following our clinical criteria. One patient became worse during treatment and required hemodialysis treatment. In the remaining patients renal function showed no deterioration even after discontinuation of the medication for several months. No serious toxic reactions were encountered. It is concluded that triple therapy is not altogether effective in reversing the clinical abnormalities associated with adult glomerulonephritis.

Resumen

Diecinueve pacientes adultos con glomerulonefritis de tipo membranoso, membrano proliferativo y proliferativo, con proteinuria severa y/o reducción en la filtración glomerular fueron tratados con una combinación de prednisona, ciclofosfamida y azatioprina por períodos de 8 a 29 meses. De acuerdo a nuestro criterio clínico ninguno de los pacientes tuvo una respuesta clínica excelente. Seis pacientes obtuvieron una respuesta buena y 13 no respondieron. Un paciente empeoró durante el tratamiento y requirió hemodiálisis. En los pacientes restantes la función renal no deterioró al descontinuar los medicamentos por varios meses. No se encontraron efectos secundarios tóxicos de estas drogas. Basados en estos estudios concluímos que la terapia triple inmunosupresora no es completamente efectiva en revertir las anormalidades clínicas asociadas con glomerulonefritis del adulto.

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HIS BUNDLE RECORDINGS IN THE CLINICAL EVALUATION OF PATIENTS WITH CONDUCTION DISTURBANCES

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His bundle electrocardiography (HBE) combined with electrical stimulation of the heart has provided a sophisticated means of evaluating the conduction system of the heart (1-2). His bundle recordings have enhanced our understanding of arrythmias (3), the Wolff-Parkinson-White syndrome (4-5) and the site of conduction abnormality in patients with various forms of heart block (6). In addition the technique has been utilized extensively to study different physiologic (7) and pharmacologic interventions in experimental animals (8-9). On the other hand, it has been stated that the usefulness of HBE in the management of patients with heart disease has been limited and that its role in the routine care of cardiac patients is yet to be determined (10).

The clinical data and follow up of the last 30 patients who had undergone HBE in our institution were reviewed with special emphasis on the contribution of this technique in the management of the patients. The following cases illustrate the potential value of His bundle electrograms in the evaluation of patients with conduction disturbances.

Methods

The technique for His bundle recordings used in our department has been previously described (11). A tripolar catheter is introduced percutaneously through a femoral vein and is positioned across the septal leaflet of the tricuspid valve. Two bipolar leads with interelectrode distances of 1 and 11 MM respectively (HBE_1 and HBE_2 leads) are recorded. In addition, two bipolar catheters with interelectrode distance of 1 MM and 1 CM are introduced through an antecubital vein and placed in the high right atrium for recording (1 MM) and pacing (1 CM). The terminals from the electrodes are fed into a distribution switch box, the outputs of which are connected to the input of the recording instrument (Electronics for Medicine, White Plains, New York). Leads 1, 2, AVF and V_1 are obtained simultaneously with the filtered (400-2000 H_2) bipolar or unipolar intracardiac leads. The stimulator used for continuous coupled or paired pacing delivered slightly underdamped pulses, 2.5 msec in duration and twice the diastolic threshold values (12). During atrial paired pacing the interval between the driving (St_1) and testing stimuli (St_2) is progressively shortened in order that the whole cycle might be scanned. His bundle pacing was performed in two of the patients reported (Cases 1 and 3). The following intervals were measured during sinus rhythm and continuous atrial pacing:

1. P-A interval (representing intra-atrial conduction time) was measured from the beginning of the P wave in the surface leads to the local atrial electrogram in the HBE leads (normal values 20-40 msec).
2. A-H interval (A-V nodal conduction time) was measured from the onset of the local atrial electrogram in the HBE lead (low right atrium) to the initial deflection of the His electrogram (normal value 50-120 msec) (11).
3. H-V interval (conduction time in specialized ventricular-Purkinje system) was measured from the initial deflection of the His electrogram to the onset of ventricular depolarization (QRS) in the surface of HBE leads (normal 35-55 msec).

Informed consent was obtained from each patient prior to the study.

Case Presentations:

Case 1-

This 69 year old male was admitted to the hospital for evaluation of dizzy spells and one syncopal episode. An electrocardiogram taken in 1969 was normal except for left anterior hemiblock. A second tracing taken in 1973 (6 months before admission) showed completed LBBB with normal axis in the frontal plane. The PR interval was 0.18 seconds. The

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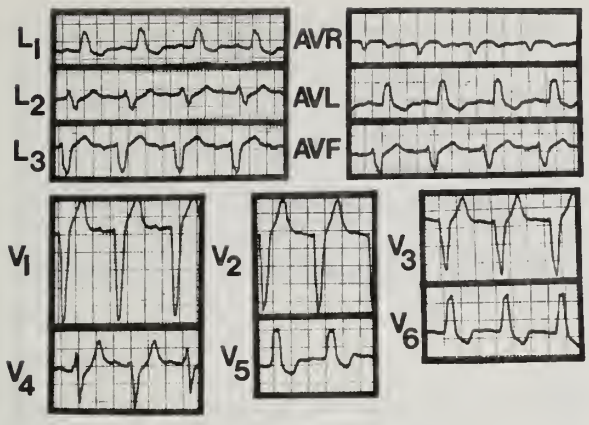


Fig. 1: *Electrocardiogram obtained at the time of admission. Complete left bundle branch block with left axis deviation is noted. The PR interval was 0.20 seconds.*

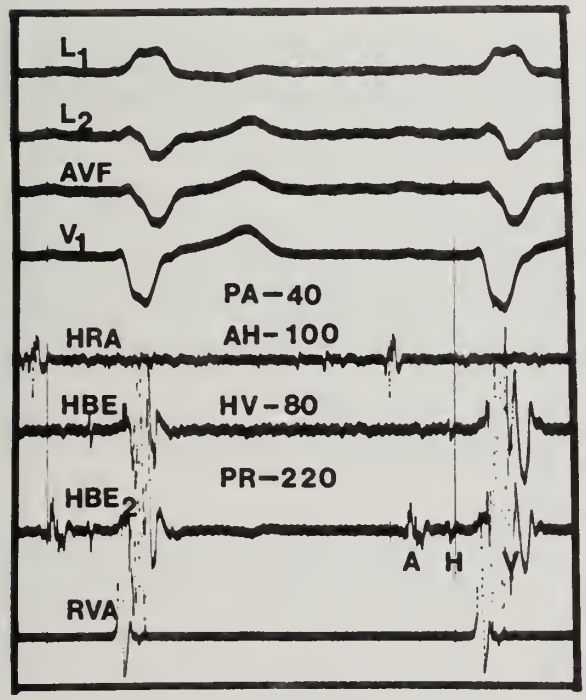


Fig. 2: *His bundle recordings revealed normal P-A and A-H intervals. The H-V interval was significantly prolonged to 80 msec. The PR interval was 220 msec, the rate 68 per minute.*

electrocardiogram at the time of admission showed complete LBBB with a QRS axis of -40 in the frontal plane (Figure 1). The PR interval was 0.20 seconds. The results of the physical examination were negative except for paradoxical splitting of the second heart sound. There was no evidence of postural hypotension or hypoglycemia. The chest x-ray revealed the heart size to be in the upper normal limits. Skull series, brain scan as well as a complete neurological work up were negative. Several 24 hour Holter monitoring studies showed sinus tachycardia with occasional premature atrial contractions.

Electrophysiological studies:

On the day of the procedure the resting sinus rate was 68 beats per minute (Figure 2). The PR interval was 220 msec. The P-A and A-H intervals were normal, however, the H-V interval was prolonged to 80 msec. During atrial pacing the patient developed block proximal to the His bundle (in the A-V node) at a pacing rate of 140/minute (normal response).

In view of the electrophysiologic findings and considering the clinical picture suggestive of episodic complete A-V block, a permanent demand ventricular pacemaker was recommended. After insertion of the cardiac pacemaker, the neurologic symptoms disappeared and the patient has been asymptomatic for 10 months.

Comments:

The important therapeutic decision taken in this patient demanded a critical review of the significance of prolonged H-V intervals in patients with bundle branch block. In these cases, H-V prolongation reflects conduction delay in the functioning bundle branch and is a manifestation of bilateral bundle branch block (6, 13). Previous reports suggest that patients with the electrocardiographic findings of bifascicular block (or partial bilateral bundle branch block) have an increased risk of developing complete atrioventricular block, which may result in transient neurologic symptoms (14-16). However, partial bilateral bundle branch block (bifascicular block) may be an incidental electrocardiographic finding and complete A-V block may never develop in patients with this pattern (17). His bundle electrocardiography allows localization and perhaps quantification of A-V conduction disturbances. Narula and Samet (18) reported marked prolongation of the H-V interval (mean of 85 msec) in patients with RBBB and left anterior hemiblock who subsequently developed higher degrees of A-V block. Our observations agree with the data presented by Scheinman et al (19) who suggested that patients with transient neurologic symptoms, bifascicular or LBBB associated with makedr prolongation of the H-V interval ($>$ 80 msec), should be seriously considered as candidates for insertion of permanent cardiac pacemakers even in the absence of documented high grade or complete A-V block.

Case 2-

A 49 year old male, with a previous myocardial infarction in 1971, was admitted to the CCU because of severe retrosternal chest pain and diaphoresis of 2 hours duration. The electrocardiogram showed an old infero-posterior myocardial infarction, narrow QRS complex, marked left axis deviation and elevation of the ST segment in the anterior precordial leads. Forty-eight hours after admission, he developed complete RBBB and a PR interval of 0.23 sec (Figure 3). His bundle electrograms recorded at the time of insertion of a temporary

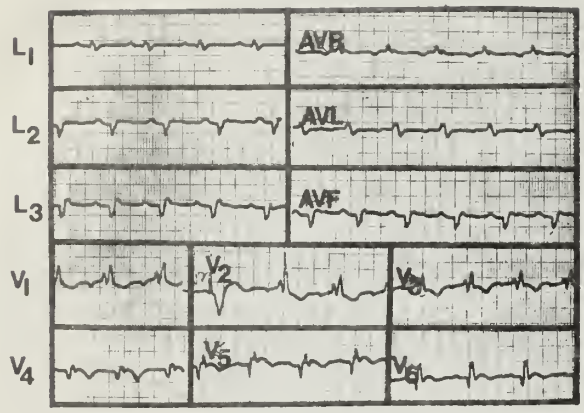


Fig. 3: *Electrocardiogram 48 hours after admission to the CCU. Complete RBBB, marked left axis deviation and prolonged P-R interval are noted. A paced beat is seen in* V_2.

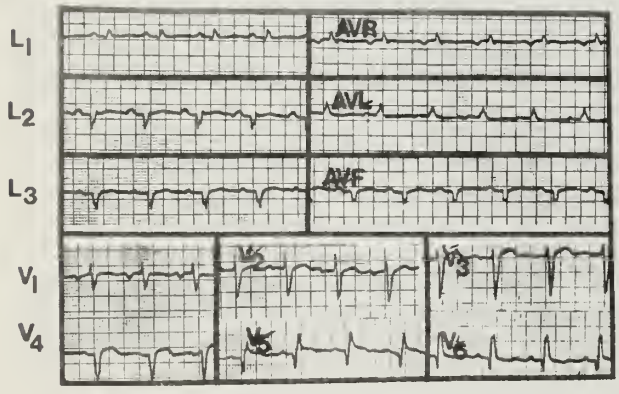


Fig. 4: *Electrocardiographic tracing recorded 14 days after admission to the CCU (12 days after insertion of temporary pacemaker). Note the prolonged PR interval, marked left axis deviation and an intraventricular conduction disturbance with a QRS complex of 0.10 to 0.11 seconds. An old infero-posterior as well as a recent antero-lateral myocardial infarction are present.*

prophylactic pacemaker revealed a prolonged H-V interval of 60 msec. Fourteen days after admission the electrocardiogram (Figure 4) showed sinus rhythm with a prolonged PR interval, marked left axis deviation suggestive of left anterior hemiblock and a recent antero-lateral myocardial infarction. The RBBB reverted to an intraventricular conduction disturbances with a QRS complex of 0.10 to 0.11 sec.

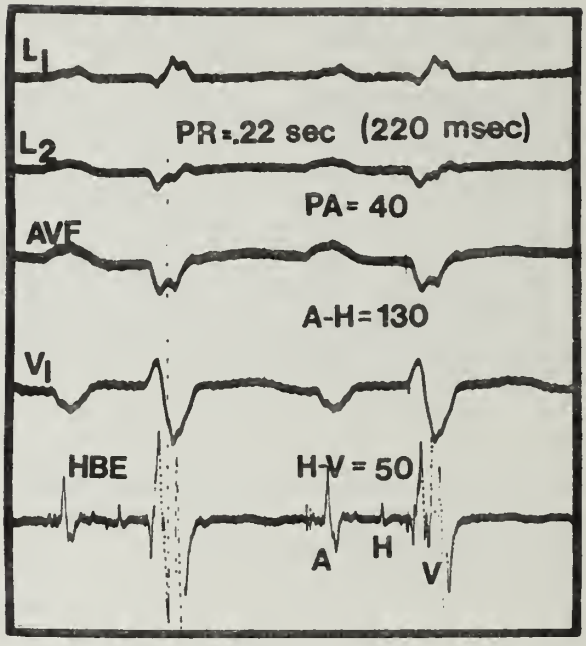


Fig. 5: *His bundle recordings 15 days after the acute myocardial infarction. The P-A and H-V intervals are within normal limits. The A-H interval is slightly prolonged. The PR interval is 220 msec.*

Electrophysiologic studies:

His bundle electrograms (Figure 5) showed normal P-A and H-V intervals. The A-H interval (A-V nodal conduction time) was prolonged to 130 mseconds. Atrial pacing up to a rate of 110 per minute showed prolongation of the A-H interval to 145 msec. No evidence of block proximal or distal to the His deflection was observed. The patient was discharged home without a permanent pacemaker, but he moved to another city three months later.

Comments:

The mortality rate associated with incomplete bilateral bundle branch block complicating acute myocardial infarction is high (20, 21). The primary cause of death has been thought to be cardiogenic shock or arrhythmias including complete heart block, asystole and ventricular fibrillation (21-22). Although the insertion of a temporary prophylactic pacemaker is still controversial, many authors recommend insertion but are aware that the benefit will be small (16, 20, 23-25).

Recent reports have suggested that His bundle recordings may be of clinical importance in patients with acute myocardial infarction complicated by incomplete bilateral bundle branch block (26). These observations suggest that those patients with bifascicular block and prolonged H-V intervals are at a higher risk for developing complete A-V block. His bundle recordings seem to be of value in determining

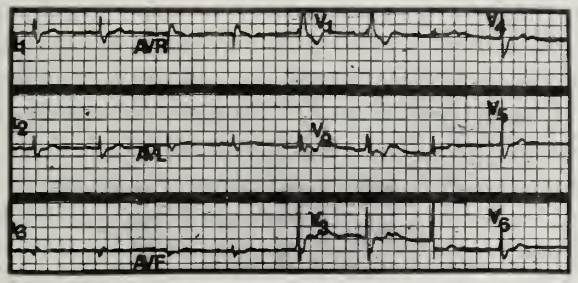


Fig. 6: *Electrocardiogram taken at the time of admission. Complete RBBB, left axis deviation and first degree A-V block are present. The sinus rate is 56 per minute.*

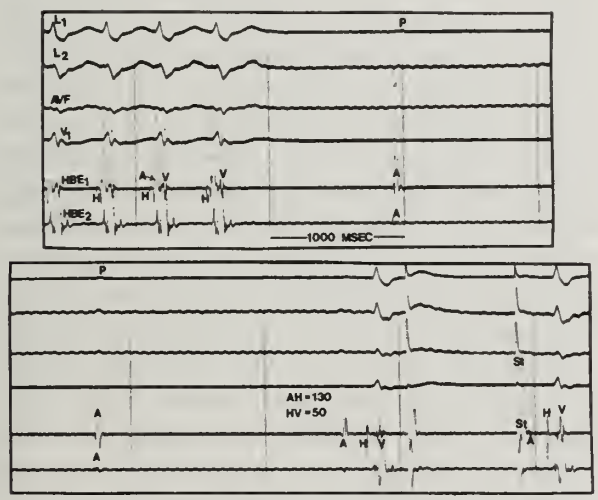


Fig. 7: *Reciprocating A-V junctional tachycardia observed at the time of the His bundle recordings; the strips are continuous. The low right atrial electrogram was lost within the ventricular deflections of the HBE lead. Immediately after the termination of the tachycardia, there was a period of A-V block during which the atrial deflections failed to activate the His bundle.*

the short term prognosis in this group of patients. The prognosis is poor for those with prolonged H-V intervals and persistent RBBB and better for those with a normal H-V interval and transient RBBB. Although it has been suggested that persistent right bundle branch block with left axis deviation in acute myocardial infarction might be an indication for permanent cardiac pacing (23, 27) further observations and controlled studies are required to validate this statement.

Considering the delayed onset and transient nature of the bundle branch block associated with a normal H-V interval (at the time of the second HBE), it is reasonable to conclude that prophylactic permanent pacing was not required in the case presented.

It is possible that serial measurements of H-V intervals during the acute stage would identify a sub group of patients that might benefit from a permanent pacemaker. More patients with acute myocardial infarction complicated by incomplete bilateral bundle branch block need to be followed up for longer periods of time to determine the effect of such intraventricular conduction disturbances on ultimate prognosis.

Case 3-

This 69 year old male was followed in the outpatient clinic because RBBB, left axis deviation and first degree A-V block (Figure 6). He was admitted for evaluation because of dizziness and fainting spells. There was no history of hypertension, diabetes or coronary artery disease. The results of the physical examination were unremarkable except for the presence of a fourth heart sound. Neurologic work up was negative. Brain scan and flow studies were suggestive of decreased blood flow in the area supplied by the right middle cerebral artery. Several 24 hours Holter monitoring studies were normal except for sinus bradycardia (56/minute).

Electrophysiologic studies:

During sinus rhythm at a rate of 60 per minute, the A-H and H-V intervals were 130 and 5 msec respectively. During atrial pacing, the patient developed reciprocating A-V junctional tachycardia (Figure 7) at a rate of 150 beats per minute. The arrythmia terminated spontaneously. Immediately after the end of the tachycardia there was a period of A-V block during which the atrial deflections apparently failed to activate the His bundle. The corresponding P-P interval preceding the first conducted sinus beat measured 1640 msec. The prolonged duration of this interval suggested the coexistence of sinus node dysfunction. During this episode, which occurred in the Cardiovascular Laboratory, the patient developed symptoms which were similar to those that he experienced before admission to the hospital.

Three explanations appeared possible to explain the symptomatic post tachycardia A-V nodal block: (a) post tachycardia induced period of abnormally prolonged A-V nodal refractoriness; (b) pseudo A-V block produced by concealed A-V junctional tachycardia and (c) bradycardia-dependent (phase 4) A-V block at the "upper" His bundle (28).

After a temporary pacemaker was inserted in the right ventricular apex, a 24 hours Holter monitoring study (Figure 8) revealed runs to supra-ventricular tachycardia at a rate of 150 per minute which terminated spontaneously, followed by sinus bradycardia and fainting spells. A permanent pacemaker was recommended because reciprocating A-V junctional tachycardias occurred in a symptomatic patient with sinus node dysfunction. Digoxin was given in an attempt to prevent the tachyarrythmias. He has been asymptomatic for 10 months.

Comments:

The reported incidence of development of heart block in

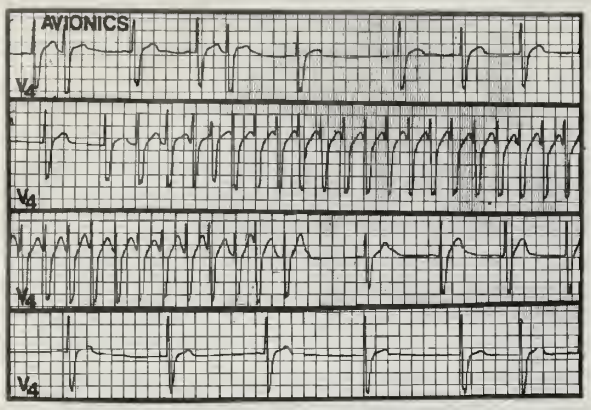


Fig. 8: *Electrocardiographic tracings obtained during a 24 housr Holter monitoring study. The strips are not continuous. A run of supraventricular tachycardia is illustrated followed by sinus bradycardia. The patient became symptomatic during these episodes.*

patients with bifascicular block, especially right bundle branch block and left anterior hemiblock has ranged from 6 to 30 percent over a period of several months to several decades (15, 16, 29). A recent prospective study on the natural history of these patients showed that progression of conduction disease was uncommon, occurring in only 6 percent of patients during a mean follow-up period of 1 1/2 years (30). In this series, patients with both normal and prolonged H-V intervals had a relatively high incidence of sudden cardiac death which could have been secondary to progression of conduction disease or ventricular fibrillation (30). Watanabe et al (31) recently reported a higher incidence of ventricular arrhythmias in patients with intraventricular conduction and when these are subjected to graded exercise, they manifest premature atrial and ventricular beats and occasionally ventricular tachycardia (32). In the case presented, symptoms could have been due to complete A-V block or to ventricular tachycardia. Sinus node dysfunction and reciprocating A-V junctional tachycardia were not suspected to be the contributing factors accounting for his clinical presentation. The information derived from His bundle electrocardiography was useful in the management of the patient and provided possible mechanisms which could be useful in understanding the genesis of symptomatic post tachycardia A-V block in patients with tachycardia-bradycardia syndrome.

Discussion

His bundle electrocardiography has been primarily considered a research technique useful in studying the conduction system of the heart and the effects of pharmacologic and physiologic interventions on A-V conduction. At the present time there are several clinical situations where critical information can only be obtained through His bundle recordings. As demonstrated in Case 1, His bundle recordings appear to be of clinical value in patients with neurologic symptoms and bundle branch block. Scheinman et al (19) reported three groups of patients with bundle branch block, dizziness, seizures or syncope and the presence of 1:1 antegrade A-V conduction at the time of the His bundle recordings. None of the patients studied had evidence of an acute myocardial infarction. In six patients neurologic symptoms were observed in the absence of electrocardiographic evidence of A-V block. The H-V interval in this group of patients was normal or minimally prolonged (mean 56 ± 9). In six other patients, the cause of the symptoms was not clear, however, in three patients the symptoms were of sufficient concern to merit implantation of a permanent cardiac pacemaker. Two of these patients experienced relief of symptoms suggesting that they were in fact related to transient bradyarrhythmias. The mean H-V interval in this group was 64 ± 11 msec. In seven other patients complete A-V block was documented as the cause of the symptoms. The H-V interval was significantly prolonged in every patient, with a mean value of 89 ± 20 msec. All patients with presumed or documented episodes of high grade A-V block had abnormal H-V intervals and six of the nine patients had H-V intervals over 80 msec. The significantly greater H-V interval in patients with documented A-V block, suggested that the specialized ventricular conduction system is involved in a progressive disease process the end stage of which results in complete A-V block (19). On the other hand, previous studies have demonstrated that a normal H-V interval in patients with bundle branch block does not preclude development of complete A-V block (33). In view of this, it remains to be determined if His bundle electrocardiography can provide a means to quantitate A-V conduction disturbances.

The indications for permanent cardiac pacemakers after an acute myocardial infarction remain a controversial issue (16, 23, 27, 34). Atkins et al (27) reported 16 patients with acute myocardial infarction and RBBB-LAD. Twelve patients had complete heart block in the first 48 hours, one of these patients died and 11 were temporarily paced. The pacemakers were removed in 7 of the 11 patients after reversion to sinus rhythm. Eight patients died suddenly and unexpectedly between 2 weeks and 4 months after the infarction. Seven of these had transient heart block during the acute stage

and 3 patients had documented recurrent complete heart block. On the basis of this data they suggested that persistent RBBB with LAD in acute myocardial infarction might be an indication for permanent pacemakers. Later Scalon et al (16) and Godman et al (22) described seven patients with RBBB-LAD who had transient complete heart block during an acute myocardial infarction; six of these patients died within eight months. Considering these reports and in view of their previous experience, Atkins et al (23) later restricted their recommendation to the group of patients with persistent RBBB-LAD who had developed transient complete A-V block during the acute stage of myocardial infarction. They found that 11 of 13 patients who did not have a permanent pacemaker died within 8 months of discharge, whereas 8 with permanent pacemakers were still alive. The possibility that sudden death might have been secondary to ventricular fibrillation during an acute ischemic episode was considered in a recent reappraisal of their report (34). At the other end of the spectrum, Waters and Mizgala (34) recently reported their experience with 27 patients with acute myocardial infarction complicated by incomplete bilateral bundle branch block, treated with temporary transvenous pacemakers. Twelve of the 27 patients died in the hospital. Progression to complete heart block occurred in 9 of the 12 patients. Fourteen of the 15 survivors have been followed up an average of 16.7 months after infarction and none had developed complete heart block. In 7 of the survivors, follow up studies indicated a trend toward regression of the conduction disturbances. The authors did not believe that the occurrence of transient complete heart block in patients with an acute myocardial infarction complicated by incomplete bilateral bundle branch block is an indication for permanent pacemaker insertion. In view of these conflicting observations it is reasonable to examine the value of His bundle electrograms in relation to the short term prognosis in this group of patients. In the series reported by Lichstein et al (20) and Lie et al (26), His bundle recordings were made in 40 patients at the time of temporary pacemaker insertion. Twenty-one of the 27 patients with bifascicular block and prolonged H-V interval died in comparison to ten deaths in 23 patients with bifascicular block and a normal H-V interval. A very interesting observation can be made by analyzing the data reported by Lichstein et al (20). Of the patients with an abnormal H-V interval (55 msec or greater) 8 died and 3 survived. In this group, there were 5 patients with H-V intervals of 70 msec or greater (range 70-100 msec), all of them died. All of the 6 survivors had H-V intervals less than 70 msec (range 45-65 msec). Although further observations and controlled studied are needed, this preliminary data suggests that His bundle recordings provide an important tool that might be used to quantitate A-V conduction disturbances. Whether permanent cardiac pacing is indicated in the group of patients with abnormal H-V intervals remains to be determined.

As we expand our understanding of the pathophysiology of conduction disturbances and cardiac arrythmias, the information derived from His bundle recordings will become more useful in the management of patients with intraventricular conduction distur-

Acknowledgment

We would like to acknowledge Benjamín Scherlag, Ph.D. for his helpful criticism and the cooperation of Miss Bonnie Agnell for the typewritten preparation of the manuscript.

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THE TOXICOLOGY OF THE PHENOTHIAZINES

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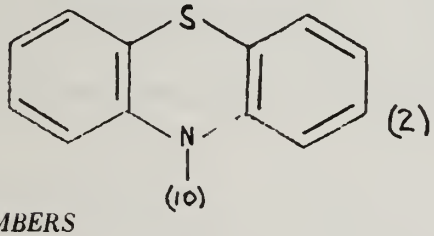
The phenothiazine group of drugs is a very effective major tranquilizer. It played a major role in changing the pattern of treatment, and the "life style" of the psychiatric patient. Much less restraint or detention is now required; and this permits considerably more treatment on an outpatient basis with excellent results.

Since so many millions of doses are now prescribed, it should be no surprise that they are found in so many homes and that frequently questions of overdose or side reactions occur.

Because of the uncertainties (sometimes) in the rapid diagnosis and management of overdose or side reactions, a brief resumé of the Toxicology of the Phenothiazines is offered:

A. *BASIC STRUCTURE*

Phenothiazine nucleus



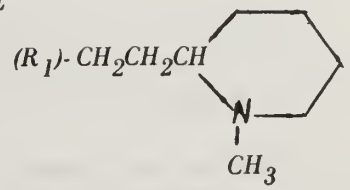
B. *MEMBERS*

Position 10 - side chain

I. DIMETHYL $(R_1)\text{-}CH_2CH_2CH_2\text{-}N(CH_3)_2$

II.PIPERAZINE $(R_1)\text{-}CH_2CH_2CH_2\text{-}N$  $N\text{–}$

III.PIPERIDINE



(See list on next page)

C. *MLD:*

Fatal (acute) dose varies widely with derivative. Approximately 15-150 mg/kg, is suggested, although severe symptoms have developed with less (2).

D. *PHARMACOKINETICS:*

Absorbed easily and quickly and is generally distributed widely. Rapidly becomes protein bound; partly destroyed in the liver and partly eliminated as the sulfoxide derivative in the urine (1). Fairly rapid onset of action, and it may still be detected in tissue even several weeks or more after high intake (9).

E. *GENERAL SIGNS AND SYMPTOMS TO OVERDOSE (1, 2, 3, 4, 5):*

CNS depression, sedation, drowsiness, ataxia, apathy, nausea, fever, antiemetic, anticholirnegic: Dilated pupils, blurred vision, dry mouth, urinary retention, tachycardia. Chilliness, constipation, stuffy nose, hypotension, coma, edema, EKG changes, ventricular arrhythmias. respiratory depression.

Stimulates the extrapyramidal system (Parkinsonism); depresses the hypothalamus; and convulsions occur with very high doses.

From the School of Medicine, Institute of Legal Medicine, University of Puerto Rico.

In partial fulfillment of the requirements for the MSc. in Toxicology; the Department of Pharmacology and Toxicology, and the Institute of Legal Medicine, University of Puerto Rico.

	Position 2 X -	Approximate (1) oral dose
I. DIMETHYL		
(1) Chlorpromazine - HCl (Thorazine) most widely used	chlorine	10 - 100 mg, tid
(2) Promazine - HCl (Sparine) weaker than chlorpromazine; less jaundice but more agranulocytosis (1)	none	50 - 100 mg, tid
(3) Triflupromazine - HCl (Vesprin) generally more potent than above two	fluorine	10 mg, tid
II. PIPERAZINE Generally cause more extrapyramidal tract symptoms, but less agranulocytosis and jaundice than chlorpromazine.		
(1) Prochlorperazine maleate (Compazine)	chlorine	10 - 30 mg, tid
(2) Perphenazine (Trilafon)	chlorine	4 - 8 mg, tid
(3) Fluphenazine - HCl (Prolixin) (Permitil)	fluorine	0.5 - 3 mg, tid
(4) Trifluoperazine - HCl (Stelazine)	fluorine	2-5 mg, tid
(5) Thiopropazate - HCl (Dartal)	chlorine	10 mg, tid
(6) Carphenazine maleate	COC_2H_5	25-50 mg, tid
III.PIPERIDINE		
(1) Thioridazine (Mellaril) generally better suited in Geriatrics and produces relatively little extrapyramidal toxicity and no reported jaundice or agranulocytosis (I)	sulfur	25-150 mg, tid
(2) Mesoridazine (Serentil) more potent than Mellaril; more likely to produce hypotension	sulfur	25-75 mg, tid

(3) Mepazine - HCl (Pacatal)	none	25 mg, tid
IV. ANTIEMETICS (many of the above plus)	chlorine	5 mg, tid
(1) Pipamazine (Mornidine)		
(2) Thiethylperazine (Torecan)	SO_2-C_2H_5	20 mg, daily
V. ANTIPRURITICS (some of the above plus)	none	2.5 mg, tid
(1) Trimeprazine (Temaril)		
(2) Methdilazine - HCl (Tocaryl)	none	8 mg, tid

Synergistic action with other CNS depressants such as alcohol, morphine, barbiturates, other hypnotics, analgesics and general anesthesia (3).

F. GENERAL SIDE REACTION (1, 2, 3, 4):

(1) Bone marrow depression with agranulocytosis: More frequent with the chlorpromazine group (but rare); less common with prochlorperazine group; no reported cases in the thioridazine group.

(2) Extrapyramidal tract symptoms: Withdraw drug, and control with anti-Parkinson drugs. Incidence is more common with the young and aged and also more usual with the females.

(a) *Parkinsonism* (1, 2, 3, 4, 6)

This condition is usually been in the aged and may be patient related and dose related and can occur at any time after conventional dosage. However, the larger the dose, the greater the incidence of occurring. The signs are similar to the classic illness - ie - reduction in facial movements, and arm movements followed by the typical shuffling gait and pill-rolling hand movements, tremulousness (spastic-jerky constant movements at rest).

(b). Acute dystonic reaction (6)

This condition comes on suddenly and consists of bizarre muscle spasms that could be confused with tetany or hysteria. The muscles of the head and neck are mostly affected producing an involuntary spasm of tongue and mouth muscles. These spasms may affect speech and swallowing; the mouth may be clamped shut and facial grimacing is observed. There may also be spasm of the external ocular muscles with persistent painful upward gaze (for minutes to hours). The arms and leg muscles although less frequently affected, can produce bizarre gait and difficulty in walking.

This acute reaction usually occurs 24 to 48 hours after starting medication. This can be dose related and is noted to occur more often in the young and in the males.

These reactions although acute, and violent in appearance are easily treated by parenteral administration of antihistaminics, barbiturates, and anti-Parkinsonism drugs. Response is usually dramatic.

(c). Akathisia (6)

There is a desire to be in continuous motion with restlessness, agitation, and an inability to sit or stand still. This may occur near the onset of treatment and therefore can easily be confused with a psychotic agitation, which could lead to continued or increased dosage.

Anti-Parkinsonism agents may produce an immediate response.

(d) Tardive dyskinesia (6)

Can appear within a month or more of

medication, but more usually it occurs after several years of treatment. It is more frequent in the elderly and in women, and with patients with a history of some brain injury.

The most frequent signs are the "bucco-linguo-masticary triad" - ie - sucking and smacking movements of the lips, lateral jaw movements and puffing of the cheeks, with the tongue thrusting, rolling or making fly - catching movements. This may be done with the mouth closed - the tongue hits the inside of the cheeks and a chewing the cud type of movement is seen.

Sometimes there is a tic-like movements of the lips and eyes; rocking, swaying or restless limb movements may precede this. Symptoms of Parkinsonism also can coexist with tardive dyskinesia.

Tardive dyskinesia which has a *very* late onset should not be confused with *acute dystonic* reaction which has a rapid onset. In many cases the tardive dyskinesia will be masked during dosage and thus will only be seen when the drug is stopped or dosage is markedly reduced. The reaction will be again masked when the drug dosage is resumed, and may get worse during emotional stress and disappear during sleep. Persistence of the symptoms after the drug is discontinued are characteristic manifestations.

The phenothiazines are an excellent antipsychotic - but should not be given "indiscriminately" to the elderly (women especially)*.

For more details on the above side reactions, one is referred to the excellent article by the Task Force of the Federal Food and Drug Administration and the American College of Neuropharmacology (6).

(3) Hypotension: May be more marked especially when given parenterally; or in patients who received general anesthesia following Chlorpromazine administration (3).

(4) Hepatitis: (Intra-hepatic obstructive jaundice (1).

Chlorpromazine (Thorazine) group is more frequently involved.

Prochlorperazine (Compazine) group is less frequently involved.

Thioridazine (Mellaril) group is least frequently involved.

(5) Dermatitis is possible with exposure to sun (photosensitive).

** - Thioridazine (Mellaril) is perhaps the safest for the elderly.*

G. POTENCY:

(1) The piperazine (prochlorperazine, Compazine) are generally more potent.

(2) The piperidine group is generally less potent and less toxic.

(a) Thioridazine (Mellaril) produces relatively little extra pyramidal toxicity and no reported jaundice or agranulocytosis; dermatitis is rare, but pigmentation of the retina has been reported by excessive use (1).

(b) Mepazine may occasionally cause agranulocytosis and hepatitis (1).

Potency (in general):

In position 2

(a) Chlorine is more potent than H.
(b) Fluorine is more potent than Cl.
(c) Sulfur is less potent than chlorine or fluorine.

H. REMARKS:

The phenothiazine group depresses the central nervous system. It enhances or potentiates the effect of (some) other central nervous system depressants and therefore should not be used in conjunction with morphine (other similar narcotics), barbiturates (other similar hypnotics), alcohol, or antihistaminics. Avoid pre-operative use because severe hypotension has occurred during general anesthesia (2).

There is no apparent drug abuse, or any accompanying "evil" effects in spite of its great use. There is no "drug dependency" or withdrawal symptoms as such. However, abrupt withdrawal of drug following high dose therapy can produce discomfort and symptoms such as gastritis, nausea, vomiting, dizziness and tremulousness. This can be avoided or minimized by a gradual withdrawal of drug, or by concomitant anti-Parkinsonism agents (7).

Side effects (drug reactions can be serious).

Members of the piperazine group are generally more potent and toxic; produce more extra pyramidal symptoms but less agranulocytosis and hepatitis. The aged (women) and children are more likely to show the dyskinesia effects.

The dimethyl group is generally less potent or toxic. Fewer extrapyramidal effects but some danger of agranulocytosis and hepatitis.

The piperidine group is generally least toxic, producing fewer of the above side reactions.

There has been the occasional report of "sudden death" with phenothiazines in patients. In some cases the cause appeared to be asphyxia due to failure of the cough reflex, in others the cause was not clear (7).

I. IDENTIFICATION:

Phenothiazines are insoluble in chloroform. Blood is not as satisfactory as *urine* for rapid identification. The phenothiazines become proteinbound and requires *strong* alkali to free it in urine or tissue. Use sodium hydroxide - ether - extraction and this should be done without delay because of possible deterioration in tissue (5). An acid hydrolysis of urine prior to extraction greatly improves sensitivity (9).

Simple, direct tests are very satisfactory for rapid emergency identification. Just because a test is rapid, simple, requires no sophisticated instrumentation and is very inexpensive to perform - does not mean that it is not reliable.

(1) One (1) ml of fresh urine plus 1 ml of FPN reagent (Reagent: 45 ml of 20 percent perchloric acid, plus 50 ml of 50 percent nitric acid, plus 5 ml of 5 percent ferric chloride; solution is stable for years) (8) → produces within *20 seconds* a faint pink (for about 30 mg dose); to a dark puple (for about *800 mg dose)* (2). Mellaril produces a bright *blue* color in the low doses, and a dark blue in the higher doses.

(2) One (1) ml of fresh urine plus 10 drops of sulfuric acid plus 1 drop of ferric chloride (10 percent) → lilac color. Salicylates in small amounts - do not interfere.

(3) More detailed quantitative tests by UV spectrophotometry, thin layer chromatography, and by gas chromatography, have been described (5, 9).

J. TREATMENT:

Withdrawal of drug*, gastric lavage, intestinal purge with saline cathartics; try emetics, but they may not work due to antiemetic action of the phenothiazine. Keep patient in horizontal position to minimize postural hypotension. Maintain heat, water, and electrolyte balance.

Combat shock; the use of sympathomimetic amines (levarterenol, etc.) is contraindicated (2). Convulsant stimulants are to be avoided. Control convulsions or excitement carefully with shortacting barbiturates; avoid other depressants (2).

There is no specific treatment, other than symptomatic and supportive.

Supportive measures for possible liver damage and agranulocytosis. Parkinson-like symptoms may be relieved with anti-Parkinsonism drugs.

Thorazine (and others) are strongly bound to blood proteins, and dialysis has been reported as not very effective.

Summary

The phenothiazine group of drugs is a very effective major tranquilizer and many millions of doses are regularly prescribed. Questions of drug overdose or drug side reactions occur. Because the diagnosis is not always simple, we have prepared this brief resumé of some of the properties, potency in relation to its structure, signs and symptoms, toxicity, possible "wierd" side effects and suggested treatment.

It is urged that the simple (one step) urine test be available in the Emergency room. This is a good presumptive test and can be performed by anyone, anywhere, at anytime*. This simple test can be very helpful in the diagnosis of an overdose or a "wierd" side reactions to the phenothiazines.

Resumen

Las fenotiazinas como grupo principal de drogas son muy efectivas. Grandes dosis son recetadas a menudo; debido a esto, problemas de sobredosis y reacciones secundarias se presentan con mucha frecuencia. El diagnóstico de sobredosis a veces resulta difícil y este artículo incluye un breve resumen de las propiedades químicas, de su efectividad en relación a su estructura molecular, señales y síntomas, toxici-

** - Except in Tardive.*

** - The FPN reagent is simple and inexpensive to prepare. This reagent is available to hospitals and clinics and can be picked up at the Institute of Legal Medicine at no expense.*

dad, posibles efectos secundarios y tratamiento de estas drogas tranquilizantes.

Se sugiere que cada sala de emergencia en los hospitales tengan a mano la solución de FPN* para determinar la presencia de estas drogas en la orina. El análisis es muy sencillo y puede ser de gran ayuda en el diagnóstico de sobredosis y reacciones secundarias de estas drogas.

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** - La solución FPN es muy sencilla y rápida de preparar; muestras de ésta para hospitales y clínicas se pueden obtener en el Instituto de Medicina Legal.*

FORO DE MEDICINA NUCLEAR *

METASTATIC BONE TUMOR

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Andrés Acosta Otero, MD

** - Esta sección que se publicará regularmente en el Boletín es auspiciada por la Sección de Medicina Nuclear de la Asociación Médica de Puerto Rico, la Sociedad de Medicina Nuclear de Puerto Rico y la Sección de Medicina Nuclear del Departamento de Ciencias Radiológicas de la Escuela de Medicina.*

Estas breves comunicaciones están encaminadas a ilustrar mediante la descripción de casos individuales la utilidad de diversos métodos nucleares en el diagnóstico médico. Siguiendo la tradición del Boletín nos hemos tomado la libertad de emplear dos lenguajes.

Case Summary

A 56-year old male entered the San Juan Veterans Administration Hospital on August 1, 1973 as a transfer from another institution where a histological diagnosis of carcinoma of the prostate had been established. Bilateral orchiectomy had been performed and treatment with diethylstilbesterol was commenced. Upon arrival he complained of asthenia, low back pain and a weak urinary stream.

Rectal examination revealed an enlarged, nodular, hard prostate. Needle biopsy showed well differentiated carcinoma.

Serum alkaline phosphatase was 91 mU/ml: prostatic acid phosphatase was 0.4 SJR units/ml.

Urogram (Figure 1) showed bilateral hydronephrosis, narrowing of the ureters at their entrance into the bladder, trabeculation and deformity of the latter. The right ureter was short and the corresponding kidney was low in position.

Bone survey demonstrated osteoblastic lesions in the pelvis and the fifth lumbar vertebra.

Skeletal scan (Fig. 1, right) (^{99m}Tc diphosphonate) detected multiple regions of increased activity in the pelvis, vertebrae, the ribs and the medial end of the left clavicle. The urinary bladder was enlarged and deformed and the right renal image was small and low in position.

Palliative teletherapy with ^{60}Co was given.

Discussion

Bone-seeking radiodiagnostic agents, which include ^{85}Sr, ^{87m}Sr, ^{18}F, ^{99m}Tc labeled polyphosphates, diphosphonate and pyrophosphate, localize preferen-



Figure 1: *Right side of the urogram is on left side of the illustration.*

From the Nuclear Medicine Service, and the Urology Section, Surgical Service, Veterans Administration Hospital, San Juan, Puerto Rico



Figure 2

tially in regions of increased osteoblastic activity. Considering that this is frequently provoked by a destructive (osteoclastic) process (1), augmented localization of these agents will be found in many pathological states. These include Paget's disease, osteomyelitis, primary and metastatic bone tumors, fractures and occasionally, metabolic bone disease.

The precise mechanism for localization probably varies in various pathological conditions and appears to include active incorporation of the radiopharmaceutical into the bone crystal matrix (2), their affinity for immature collagen (2) and increased blood flow (3, 4).

Because several of the bone-seeking radiodiagnostic agents are excreted by the kidneys, incidental visualization of the urinary tract may, as in this case, yield additional useful diagnostic information.

Skeletal scanning has found its greatest utility in the search for metastatic spread of tumors where it has been shown to be unquestionably superior to the traditional roentgen "bone survey" (4). It thus should be performed as part of the staging process preliminary to tumor therapy planning, particularly in cases of tumors characterized by hematogenous spread such as bronchogenic, prostate, breast and thyroid carcinoma.

References

1. *Rasmussen, H., et al:* Hormonal control of skeletal and mineral homeostasis. Amer J Med 56: 751, 1974.
2. *De Nardo, G. L., Jacobson, S. J., and Raventos, A.:* ^{85}Sr bone scan in neoplastic disease. Semin Nucl Med 2: 18, 1972.
3. *Rosenthall, L., Kaye, M.:* Technetium ^{99m} pyrophosphate kinetics and imaging in metabolic bone disease. J Nucl Med 16: 33, 1975.
4. *Blau, M., Ganatra, R., and Bender, M. A.:* ^{18}F - fluoride for bone scanning. Semin Nucl Med 2: 31, 1972.

FROM THE CHAMPUS BULLETIN - Technical Information Division, Ch. 13, Office of CHAMPUS, Denver CO 80240:

CHAMPUS Revises Prevailing Charge Formula

A revised formula for determining prevailing charges has been put into effect by officials of the Civilian Health and Medical Program of the Uniformed Services (CHAMPUS) to bring these charges in line with those of other Federal health care programs such as Medicare.

A prevailing charge is one of three factors used by CHAMPUS in setting a reasonable charge for a health care service or supply. The others are the customary charge of a provider and the actual charge. The reasonable charge is the lowest of the three. It includes both the beneficiary's share and the government's share.

All CHAMPUS payments for outpatient services or supplies and for maternity care benefits are based on a reasonable charge. Also, CHAMPUS payments for inpatient services and supplies that are not included in hospital bills are based on a reasonable charge.

According to CHAMPUS officials, the revision could affect the amount that the program pays for any special service or supply.

Under the revised formula, the prevailing charge is now set at an amount which is high enough to cover the customary charges for three out of every four bills from all doctors or other health care providers in a geographic area during the preceding calendar year for a service or supply. In technical terms, this means that the prevailing charge is set at the 7th percentile profile. Previously, it had been set at an amount high enough to cover nine out of ten customary charges.... the 90th percentile profile.

The customary charge is generally the one most frequently made by a doctor or other health care provider for a service or supply.

A change from setting a prevailing charge on the basis of the 90th percentile profile to the 7th percentile profile has created misunderstanding on the part of some beneficiaries who believe that CHAMPUS benefits have been reduced from 90 percent to 75 percent. CHAMPUS officials emphasize that this is not an accurate statement.

When prevailing charges are set by geographical areas, they may vary from one area to another.

CHAMPUS officials point out that other federal health care programs have been setting the prevailing charge at an amount just high enough to cover the customary charges for three out of every four bills. They say that the change in the CHAMPUS formula makes the program payment policy more consistent with those of other federal health care programs.

Because the change could affect the amount paid by the government for a particular service or supply, CHAMPUS officials urge that all beneficiaries make a special effort to use a doctor or another health care provider who participates in the program.

A participating provider agrees to accept the reasonable charge set by CHAMPUS as payment in full. Thus, a beneficiary is protected against responsibility for cost above his share of the reasonable charge.

A doctor or other health care provider who does not participate in CHAMPUS does not agree to accept the reasonable charge as payment in full. The nonparticipating provider's fees may be more than the reasonable charge set by CHAMPUS. A beneficiary is then responsible for his share of the reasonable charge plus any difference between that reasonable charge and the actual fee.

FROM HEW NEWS:

Regulations which would permit any State to receive Medicare reimbursement for providing specialized consultant services to skilled nursing facilities were proposed today by the Department of Health, Education, and Welfare.

To participate in Medicare, skilled nursing facilities must retain consultants in certain fields (e. g. dietary) where the facility does not employ such personnel.

Under the regulations proposed today, State Health Departments would, if willing and able to do, supply such consultants upon written request by the facility and receive Medicare reimbursement. The intent is to permit facilities to use State consultants in areas where private consultants are in short supply.

Interested parties have 30 days after today's publication in the Federal Register to submit comments.

FLEXIBLE FIBEROPTIC COLONOSCOPY - A MULTIDISCIPLINARY INTERNATIONAL SYMPOSIUM, September 22-24, 1976, Cherry Hill Inn, Cherry Hill, New Jersey. For further information contact John H. Killough, M. D., Jefferson Medical College, 1025 Walnut Street, Philadelphia, Pa. 19107, (215) 829-6992. Fee: $200.

ATENCION

Local comercial propio para oficinas de médicos, dispensario, laboratorio, Rayos X, etc. Farmacia cercana y negocios. En avenida y avenidas cercas. 67,000 habitantes. Renta a discutirse con facilidades. 1,200 pies cuadrados construídos. Inf. Sr. Pablo Alicea, Farmacia Alicea, tels. 784-7452, 784-9164, Res. 780-3769.



A Broken Heart

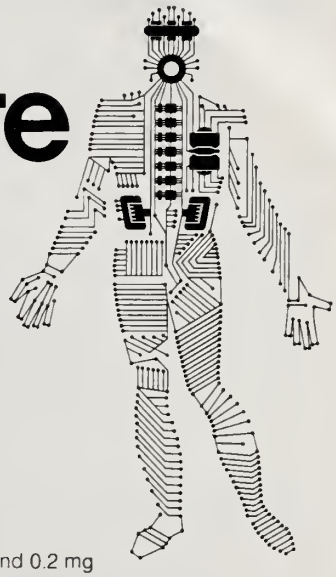
It can start with a little high blood pressure

Infarction with rupture of the wall in the left ventricle of man, 66, with mild hypertension. Blood clot in pericardial sac. Postmortem.

Photographed exclusively for Boehringer Ingelheim by Lennart Nilsson.



Reach for normal blood pressure



In mild to moderate hypertension

Tablets of 0.1 and 0.2 mg

Catapres® (clonidine HCl)

Catapres can make a diuretic look good.

When more than a diuretic is needed, adding Catapres usually lowers blood pressure more.[1]

You can add Catapres to Catapres to get pressure down near normal.

Wide therapeutic dosage range—0.2 mg to 2.4 mg* daily. Catapres may be all you need to reach near-normal levels.

*Doses as high as this have rarely been employed.

Catapres usually doesn't add a lot of problems.

The most common side effects—dry mouth, drowsiness, sedation—generally tend to diminish with time. When stopping Catapres, reduce dosage gradually over two to four days to avoid a possible rapid rise in pressure.

Please see next page of advertisement for
a brief summary of the prescribing information including
precautions, warnings, and adverse reactions.



Hypertension through the lens of Lennart Nilsson. The photographic genius of Lennart Nilsson has revealed extraordinary details of the human organism. Now, Boehringer Ingelheim has commissioned an exclusive series of photographs by Nilsson depicting hypertensive damage. This series, presented in the interest of continuing medical education, vividly records the progression of an insidious disease.

In mild to moderate hypertension

The Catapres Potential: blood pressure not just down, but down near normal

Catapres® Tablets of 0.1 and 0.2 mg (clonidine HCl)

Start with Catapres when a diuretic is wrong for your patient

Add Catapres when a diuretic alone doesn't let you reach near-normal pressure

Catapres®
(clonidine hydrochloride)
Tablets of 0.1 mg and 0.2 mg

Indication: The drug is indicated in the treatment of hypertension. As an antihypertensive drug, Catapres (clonidine hydrochloride) is mild to moderate in potency. It may be employed in a general treatment program with a diuretic and/or other antihypertensive agents as needed for proper patient response.

Warnings: Tolerance may develop in some patients necessitating a reevaluation of therapy.
Usage in Pregnancy: In view of embryotoxic findings in animals, and since information on possible adverse effects in pregnant women is limited to uncontrolled clinical data, the drug is not recommended in women who are or may become pregnant unless the potential benefits outweigh the potential risk to mother and fetus.
Usage in Children: No clinical experience is available with the use of Catapres (clonidine hydrochloride) in children.

Precautions: When discontinuing Catapres (clonidine hydrochloride), reduce the dose gradually over 2 to 4 days to avoid a possible rapid rise in blood pressure and associated subjective symptoms such as nervousness, agitation, and headache. Patients should be instructed not to discontinue therapy without consulting their physician. Rare instances of hypertensive encephalopathy and death have been recorded after cessation of clonidine hydrochloride therapy. A causal relationship has not been established in these cases. It has been demonstrated that an excessive rise in blood pressure, should it occur, can be reversed by resumption of clonidine hydrochloride therapy or by intravenous phentolamine. Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of the sedative effect. This drug may enhance the CNS-depressive effects of alcohol, barbiturates and other sedatives. Like any other agent lowering blood pressure, clonidine hydrochloride should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal failure.

As an integral part of their overall long-term care, patients treated with Catapres (clonidine hydrochloride) should receive periodic eye examinations. While, except for some dryness of the eyes, no drug-related abnormal ophthalmologic findings have been recorded with Catapres (clonidine hydrochloride), in several studies the drug produced a dose-dependent increase in the incidence and severity of spontaneously occurring retinal degeneration in albino rats treated for 6 months or longer.

Adverse Reactions: The most common reactions are dry mouth, drowsiness and sedation. Constipation, dizziness, headache, and fatigue have been reported. Generally these effects tend to diminish with continued therapy. The following reactions have been associated with the drug, some of them rarely. (In some instances an exact causal relationship has not been established.) These include: Anorexia, malaise, nausea, vomiting, parotid pain, mild transient abnormalities in liver function tests; one report of possible drug-induced hepatitis without icterus and hyperbilirubinemia in a patient receiving clonidine hydrochloride, chlorthalidone, and papaverine hydrochloride. Weight gain, transient elevation of blood glucose, or serum creatine phosphokinase: congestive heart failure, Raynaud's phenomenon; vivid dreams or nightmares, insomnia, other behavioral changes, nervousness, restlessness, anxiety and mental depression. Also rash, angioneurotic edema, hives, urticaria, thinning of the hair, pruritus not associated with a rash, impotence, urinary retention, increased sensitivity to alcohol, dryness, itching or burning of the eyes, dryness of the nasal mucosa, pallor, gynecomastia, weakly positive Coombs' test, asymptomatic electrocardiographic abnormalities manifested as Wenckebach period or ventricular trigeminy.

Overdosage: Profound hypotension, weakness, somnolence, diminished or absent reflexes and vomiting followed the accidental ingestion of Catapres (clonidine hydrochloride) by several children from 19 months to 5 years of age. Gastric lavage and administration of an analeptic and vasopressor led to complete recovery within 24 hours. Tolazoline in intravenous doses of 10 mg at 30-minute intervals usually abolishes all effects of Catapres (clonidine hydrochloride) overdosage.

How Supplied: Catapres, brand of clonidine hydrochloride, is available as 0.1 mg (tan) and 0.2 mg (orange) oval, single-scored tablets in bottles of 100.

For complete details, please see full prescribing information.

Under license from Boehringer Ingelheim GmbH

Reference: 1. Data on file at Boehringer Ingelheim Ltd.

Boehringer Ingelheim Ltd.
Elmsford, New York 10523

Breast self-examination:

KEY ROLE OF THE PHYSICIAN

item:	**Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.**
item:	**Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, *fewer than 1 in 5* women practice BSE, and *only half* have an annual breast examination by a physician.**
item:	**Only 35% of all women polled reported that a *physician* had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.**
item:	***But,* among women who received personal instruction from their physicians, the overwhelming majority *(92%)* practiced BSE during the preceding year.**

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE.

The American Cancer Society gives major emphasis to breast cancer through research and a vast array of public educational materials, designed to give women life-saving information about the disease. Our latest approach is via a pioneering television film starring Jennifer O'Neill, "Breast Cancer: Where We Are." Where we *will* be in a few years will certainly hinge on our joint efforts.

American Cancer Society®

LISTA DE ANUNCIANTES

1. BOEHRINGER-INGELHEIM

   Catapres

2. BURROUGHS WELLCOME

   Neosporin
   Septra

3. CIBA PHARM.

   Vioform-HC

4. ROCHE LAB.

   Azo Gantanol
   Bactrim
   Valium

5. ROERIG & CO.

   Antivert

6. W. H. RORER

   Maalox Plus

7. SMITH, KLINE & FRENCH

   Dyazide

8. UPJOHN CO.

   Medrol Desepak

Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

Warnings: Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

Supplied: Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

ROCHE

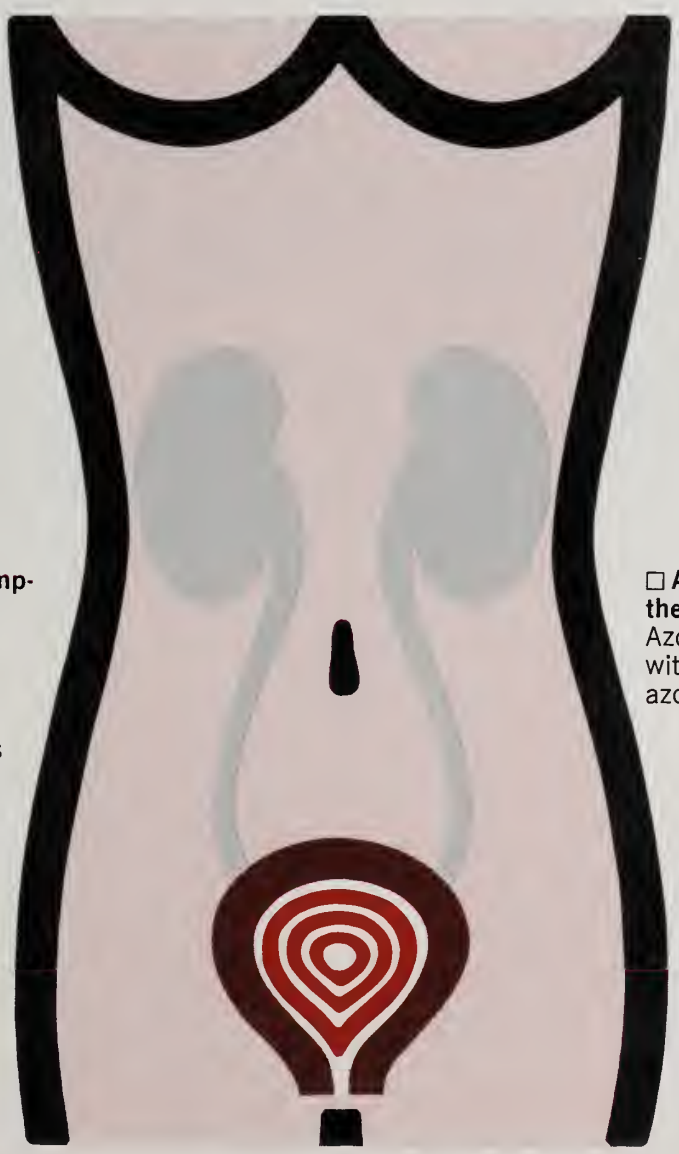
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

When pain complicates acute cystitis*

Azo Gantanol®

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

for the pain for the pathogens



☐ **Early relief of painful symptoms** such as burning and discomfort associated with urgency and frequency.

☐ **Effective control of susceptible pathogens** such as *E. coli, Klebsiella-Aerobacter, Staph. aureus, Proteus mirabilis* and, less frequently, *Proteus vulgaris.*

☐ **Appropriate antibacterial therapy:** up to three days with Azo Gantanol, then 11 days with Gantanol® (sulfamethoxazole).

*nonobstructed; due to susceptible organisms

ROCHE



Big Balanced Rock, Chiricahua Mountains, Arizona (approx 1,000 tons)

□ Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
□ Can relieve nausea and vomiting often associated with vertigo:*
□ Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
□ Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
□ Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences–National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert®/25
(meclizine HCl) 25 mg. Tablets
for vertigo*

Famous Fighters



NEOSPORIN® Ointment
(polymyxin B-bacitracin-neomycin)
is a famous fighter, too.

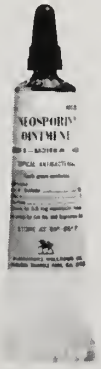
Provides overlapping, broad-spectrum antibacterial action to help combat infection caused by common susceptible pathogens (including staph and strep).

Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base), special white petrolatum qs in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: Therapeutically (as an adjunct to systemic therapy when indicated) for topical infections, primary or secondary, due to susceptible organisms, as in • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS:** Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components. **WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709



Septra DS. The same reliable formulation but doubled in tablet strength, lower in cost.

For patients with recurrent urinary tract infections

Septra DS: the same Septra efficacy in recurrent cystitis, pyelitis, and pyelonephritis due to susceptible organisms

Septra DS: the same Septra spectrum—E coli, Klebsiella-Enterobacter, P mirabilis, P vulgaris, P morganii

Septra DS: the same b.i.d. dosage schedule, but one tablet instead of two

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method *(Federal Register 37:* 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or

New Septra® DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Double Strength tablet dosage: 1 tab b.i.d.



NGS

jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **At present, data are insufficient to recommend use in infants and children under 12.**

Precautions: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Brand new... and effective for over 25 years

Great new lemon swiss creme flavor.
Proven Maalox® formula plus simethicone.

New Maalox® Plus with SIMETHICONE

ANTACID/ANTIFLATULENT

- taste preferred by over 60% of chronic antacid users tested with another leading antacid
- extra simethicone to relieve flatulence
- non-constipating
- low sodium content
- available in liquid or chew tablets

After you taste it, you'll prescribe and recommend it.



ROHER

WILLIAM H. RORER, INC.
Fort Washington, Pa. 19034

LIBRARY OF MEDICINE
BOSTON

AUG 24 1976

Boletín

asociación médica de puerto rico



THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
10 SHATTUCK STEET

Vol 68 Julio 1976 No.7

Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

THE FRANCIS A. COUNTWAY
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AUG 24 1976

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium® (diazepam) IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic anxiety states with associated depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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BOLETIN ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial Fundado en 1903

Volumen 68 Enero 1976 Número 1

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Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

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THROMBOSIS OF THE AXILLARY-SUBCLAVIAN VEIN
A REPORT OF TWO CASES

Germán E. Malaret, MD, FACP

Thrombosis of the axillary-subclavian vein is an uncommon finding. One of its causes is "Effort" thrombosis of the axillary vein, otherwise known as the Paget-Von Schroetter syndrome, an uncommon condition accounting foronly a small percentage of all thrombophlebitic episodes seen but one that must be considered whenever a venous obstructive problem of the upper extremity is identified. The use of invasive techniques is another cause for this condition.

Recently I was able to see two patients with subclavian venous thrombosis in one year. One represented the classic "effort" thrombosis or Paget-Von Schroetter syndrome whereas the other one represented one of the complications of the use of central venous catheters. They are presented here to show their similarities although their etiologies are completely different, and to awaken awareness of this uncommon problem.

Case Reports

Case 1:

GD is a 50-year old woman who came in to the office complaining of edema and pain in the right upper extremity and right side of neck. The pain had started approximately five days before and was unrelated to any "injury".

On a careful review of the history, however, she recalled carrying a very heavy movie projector for a rather "long" distance several hours before the onset of the pain. She noticed some pain when she suddenly lifted the projector and carried it to her destination. Then, about five hours or so later the pain recurred and persisted.

Initial examination revealed fullness in the right supraclavicular area with tenderness of the sternocleidomastoid insertion and marked swelling of the right upper extremity as compared to the left upper extremity. The difference between the two extremities was approximately 3 cms. at different levels in the arm and forearm and one cm. at the wrist area.

Multiple studies were done including venography (Figs. 1, 2), which demonstrated clearly the obstruction in the subclavian vein and the development of multiple collaterals. She was treated conservatively and gradually the swelling diminished although chronic edema has persisted. The pain disappeared completely within ten days.

Case 2:

The second case was FSS, a 60-year old man, who received a stab wound in the lower right side of the chest. He was treated elsewhere where a central venous catheter was inserted through the right subclavian vein. He recuperated uneventfully from his stab wound and was discharged after five days. Two



Figure 1

Presented at the Annual Scientific Session, Puerto Rico Heart Association, September, 1974.



Figure 2



Figure 3

weeks later I saw him in my office. He had developed large collaterals of the right upper extremity and right anterior and posterior chest with obvious edema in the area and swelling of the right upper extremity. It was quite clear that he had a subclavian venous obstruction perhaps even extending into the superior vena cava in view of the facial congestion and plethora. A venogram (Fig. 3) clearly showed the obstruction in the subclavian vein with the development of multiple collaterals around the obstruction.

This patient was also treated conservatively and slowly but surely the collaterals subsided as did the swelling. 18 months later, however, he still had evidence of collateral circulation and fullness of the area indicative of persistent obstruction.

Comments

These two cases clearly illustrate the effects of axillary-subclavian venous obstruction. The first one is a classical case of the effort syndrome which in this case was the carrying of a heavy movie projector by a person not used to carrying such heavy objects. The second one was a classical case of a complication secondary to a central venous catheter.

The typical clinical picture of axillary subclavian venous thrombosis is that due largely to venous obstruction with passive congestion of the extremity involved which becomes swollen, mildly to moderately painful and slightly cyanotic over a period of several hours. The skin is warm and superficial veins are distended. There may be low grade fever. The condition must be differentiated from cellulitis and lymphedema. The former is often abrupt with high fever and no venous distension whereas the latter develops slowly over weeks or months.

In a recent case report Vicens and Just Viera (1) described clearly the clinical picture of "effort" thrombosis which is primarily pain, edema and the development of collateral circulation. There are other symptoms which are variable including numbness, aching, stiffness, weakness, coldness, etc.

They also described the pathogenesis mentioning at least 15 precipitating factors in which the common denominator was severe effort. Apparently, the sudden stretching or snapping of the vein causes some damage to the intima following which a thrombus develops. There may also be local venous spasm or constriction because of muscle injury or even hematoma formation in the axillary region causing direct compression of the vein. This usually results from such actions as carrying heavy buckets or other heavy objects, throwing a ball, swimming, etc. Although multiple tests can be done the only real valuable tests, in my opinion, is venography which will clearly demonstrate the obstruction and the development of collaterals. The second most important step is to get a complete history in an attempt to elucidate the precipitating factor-as was illustrated by the first patient described.

Walters et al (2) recently described the complications of the use of percutaneous central venous catheters in 240 cases of myocardial infarction. They found that phlebitis occurred in 16 percent of the cases but only 4 patients had symptomatic subclavian vein thrombosis. In four other cases asymptomatic axillary vein throm-

bosis was shown by venography. They also concluded that anticoagulant therapy was of no value in preventing thrombus formation. It appeared that the use of central venous pressure catheters was quite safe.

The question, of course, always arises as to how frequently pulmonary emboli develop from such lesions. It is satisfying to know that they are rather infrequent but the threat of embolism, is ever present since a major vessel is involved. The main problem is the local discomfort and swelling which often incapacitates the patient temporarily, specially if the injury is in the dominant arm. Fortunately, the disability is usually of short duration, lasting only a few weeks with fairly good recovery.

Treatment consists mainly of anticoagulants, if the condition is recognized in its early stages and treatment is started immediately, although their value is debatable (2). Sympathetic block has been advocated by some because of venous spasm. Application of heat and arm elevation have been tried with variable success. Analgesics and anti-inflammatory agents such as Phenylbutazone are of value to decrease local symptoms. In most cases conservative therapy is probably sufficient since the condition tends to correct itself in a fairly short period of time. This was the case in Just Viera's patient and also in both the patients presented here.

Summary

Two cases of subclavian venous thrombosis have been presented. One is a good example of the Paget-Von Schroetter syndrome or "effort" thrombosis whereas the second one is a good illustration of one of the complications of the use of central venous pressure catheters. The main reason for presenting them is to remind the reader that this condition does occur and it must be considered whenever a patient appears with pain and swelling of the upper extremity for no apparent reason, particularly if it is one sided. If such a case presents itself and there is no obvious cause, a diligent search in the history might reveal the precipitating "effort" etiology.

Resumen

Dos casos de trombosis de la vena subclavia-axilar han sido presentados. El primero es un ejemplo clásico del síndrome de Paget-Von Schroetter en el cual la trombosis se desarrolló como resultado de "trauma por esfuerzo". El segundo ilustra una de las complicaciones del uso de catéteres endovenosos para medir la presión central venosa. La razón principal para presentar estos dos casos es recordarle a los lectores que este tipo de oclusión venosa ocurre y se debe considerar en el diagnóstico diferencial de cualquier paciente que se presente con dolor y edema de las extremidades superiores sin explicación aparente, particularmente si es unilateral. En tales casos se debe revisar el historial cuidadosamente para determinar si ha habido "trauma a esfuerzo".

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NIVELES NORMALES DE T-4 TOTAL Y T-3 TOTAL POR TECNICAS DE RADIOINMUNOENSAYO EN LA PRIMERA SEMANA DE VIDA

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Ivelisse Lang de Ferriol, MT
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Las diferencias que existen en los niveles normales de hormonas tiroideas circulantes entre los adultos y los recién nacidos, nos obligan a determinar los valores normales para la edad, según los métodos de estudio empleados. En un estudio previo, establecimos por vez primera, de forma longitudinal en niños, los niveles circulantes de tiroxina total (T-4), captación de T-3 en resina e índice de tiroxina libre, mediante técnicas de radioensayo en columna (1-2). Los niveles de TSH en el primer mes de vida también constituyen tema de otras publicaciones (2-4).

Esta comunicación establece de forma longitudinal, los niveles circulantes normales de triiodotironina total y tiroxina total, empleando técnicas nobeles y más exactas de radioinmunoensayo.

Métodos de Estudio

Se emplearon las muestras de sangre obtenidas en recién nacidos a término, sin aparentes complicaciones, y que fueron los sujetos de un estudio previo (1). Se excluyeron los prematuros, los niños de bajo peso al nacer, recién nacidos con complicaciones perinatales y los hijos de madres con síndrome nefrótico, endocrinopatías o que recibían terapia hormonal.

Se hicieron determinaciones de tiroxina total y de triiodotironina total en 14 niños, 4 hembras y 13 varones, a las edades de 0-24 horas, 48-72 horas y una semana de vida.

Los niveles de tiroxina total fueron determinados utilizando una técnica de radioinmunoensayo con I^{125} de la Compañía Diagnostic Products Corporation *, que mide los niveles circulantes de L-tiroxina, la cual no requiere extracción cromatográfica previa. La concentración de T-4 se mide en el suero del paciente, de forma directa, utilizando ácido 8-anilino-1- naftaleno - sulfónico (ANS) y barbital sódico, para bloquear el ligamiento de T-4 a la globulina ligadora de tiroxina (TBG) (5, 6) y a la prealbúmina ligadora de tiroxina (TBPA) (7). La técnica consiste de los siguientes pasos: a) competencia del T4 sérico y el T4 I^{125} por el anticuerpo específico en presencia de ANS y barbital: b) separación del T-4 libre y el ligado con gama globulina de cabra anticonejo: y, c) recuento del T4 I^{125} ligado al anticuerpo empleando un contador de radiaciones gama adecuado. El valor normal aceptado para adultos es de 5.5 - 14 ug/dl.

Los niveles de triiodotironina (T-3) por radioinmunoensayo, fueron realizados con la técnica desarrollada por la compañía Diagnostic Products Corporation *, que mide los niveles circulantes de 3, 5, 3' -L-triiodotironina (T-3), la cual no requiere extracción cromatográfica previa. La triiodotironina se mide directamente en el suero del paciente, utilizando ANS para bloquear la interacción de las hormonas tiroideas y las proteínas séricas (5). El procedimiento consiste de los siguientes pasos: a) Competencia del T-3 sérico y el T-3 I^{125} por el anticuerpo específico en presencia de ANS; b) separación del T-3 libre y el ligado mediante el empleo de gamaglobulina de cabra anticonejo: y, c) recuento del T3 I^{125} ligado al anticuerpo con contador de radiaciones gama adecuado. El valor normal aceptado para adultos es de 80-180 ug/dl.

Las muestras fueron procesadas todas a la misma vez para evitar variaciones entre ensayos. Todas las muestras fueron corridas en duplicado. Para medir las radiaciones del I^{125} utilizamos el contador de radiaciones gama de 3 canales, Bio-Gamma, de la Casa Beckman.

Los reactivos fueron obsequio de la compañía Diagnostic Products Corporation.

Resultados

La Tabla I muestra el valor promedio, la desviación

---

* - *Diagnostic Products Corporation, 12306 Exposition Boulevard, Los Angeles, California 90064.*

De la Sección de Endocrinología Pediátrica y Genética Médica, y del Laboratorio de Endocrinología y Genética Médica, del Hospital Dr. R. E. Betances, Centro Médico de Mayagüez.

TABLA I
NIVELES NORMALES DE HORMONAS TIROIDEAS EN LA PRIMERA SEMANA DE VIDA, DETERMINADAS POR TECNICAS DE RADIOINMUNOENSAYO (RIA)

Muestra *	0-24 hrs.	48-72 hrs.	1 semana
T3 RIA			
$\bar{X}$	150.89	77.11	110.39
S.D.	76.56	58.91	73.50
R.	0.-304.01	0.-194.93	0.-257.39
ng/dl			
T4 RIA			
$\bar{X}$	20.07 ug/dl	19.5 ug/dl	16.91 ug/dl
S.D.	6.33	5.39	4.65
R.	7.41-32.73	8.72-30.28	7.61-26.21

$\bar{X}$ = media S. D. = Desviación Estandar R = Fluctuación (range)

* n = 14 = $\bar{X} \pm 2$ S.D.

TABLA II
NIVELES DE T_3 TOTAL Y T_4 EN LAS PRIMERAS 24 HORAS DE VIDA

Muestra	< 12 hrs. *	> 12 hrs. *
T_3 RIA		
$\bar{X}$	87.21	214.57
S.D.	36.85	47.49
R	160.91	119.59 - 309.55
ng/dl		
T_4 RIA		
$\bar{X}$	16.5	23.57
S.D.	2.61	7.16
R.	11.28 - 21.72	9.25 - 37.89

* n = 7

estandar y la fluctuación ("range") de los valores obtenidos para tiroxina total y triiodotironina total y triiodotironina total en la primera semana de vida. Debido al número pequeño de la muestra, ambos sexos se consideran juntos para efectos estadísticos.

Se observa que los niveles de T-4 total son más altos

en las primeras 24 horas de vida, disminuyendo luego. Durante la primera semana de vida, el valor promedio es mayor al aceptado como normal en adultos.

Los niveles de T-4 son mucho más altos en el grupo donde se obtuvo la primera muestra entre las 12-24 hrs. de edad. El número de la muestra es pequeño (7 por subgrupo) por lo que no podemos hacer inferencias estadísticas (Tabla II).

Los niveles de T-3 total son mayores en las primeras 24 horas de vida, disminuyendo durante las primeras semanas de vida. Todos los valores caen dentro de los límites aceptados para los adultos. Al comparar los subgrupos de las muestras en las primeras 24 horas, observamos que los niveles de T-3 son mucho más altos en los niños mayores de 12 horas, tal como ocurre con el T-4 total.

Discusión

Este estudio confirma nuestros hallazgos previos (1-4) de un estado de hipersecreción tiroidea fisiológica en los primeros días de vida. Demostramos que hay una secreción "normal" de triiodotironina e hipersecreción de tiroxina en el período neonatal. Se observa que la hipersecreción es mayor en los sujetos mayores de 12 horas de vida. A pesar de que el número de sujetos es menor, se confirman los hallazgos previos, los cuales son secundarios a hipersecreción de TSH en el período neonatal (3-4).

Av Ruskin y colaboradores, demostraron previamente, en un estudio seccional realizado en Nueva York, que los niveles de triiodotironina total por técnicas de radioinmunoensayo en niños de 3 días de edad, caían dentro de los límites normales para adultos. Observaron un valor promedio de 140± 16.2 ug/dl comparando con otras edades, llegan a la conclusión que los niveles de triiodotironina total son bastante similares, no observando diferencia de sexo o edad (8).

En nuesdro estudio se establecen los niveles normales de triiodotironina total y de tiroxina total por técnicas de radioinmunoensayo, para una población de recién nacidos a término normales. Consideramos que estos valores habrán de ser útiles a los que evaluen la función tiroidea en recién nacidos con técnicas de radioinmunoensayo. Todo ello adquiere importancia ahora que la determinación de niveles de hormonas tiroideas en recién nacidos se hace cada vez más frecuente, y en una prueba obligada de discerninmiento en todos los recién nacidos, como ya comienza a serlo en algunos estados de los Estados Unidos de Norteamerica.

Resumen

En este estudio se establecen los niveles normales de triiodotironina y tiroxina total por técnicas de radioinmunoensayo, en una población de recién nacidos a término normales. Se confirman los hallazgos de estudios previos de una hiperfunción tiroidea fisiológica en el período neonatal.

Summary

This paper presents the normal circulating levels of total thyroxine (T-4) and total triiodothyronine (T-3), during the first week of life, in a normal puertorrican full term population. As in previous studies (1-4), a physiologic hyperthyroid state is observed in the first week of life. Even though that the sample is small, highest levels of T-3 and T-4 are observed in children over 12 hours of age when the first 24 hrs. age period is evaluated. Circulating T-3 levels fall in the normal adult range.

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LA SENSIBILIDAD DE LA FUNCION ANTITOXICA HEPATICA DEMOSTRACION EXPERIMENTAL

Angel Rodríguez Olleros, MD
René Dietrich, MD
J. E. Taveras, MD

l hígado es el órgano "aduanero" de la nutrición del cuerpo, por lo tanto es lógico que evidencie su estado de función frente a "tóxicos" potenciales que en pequeñas dosis se usan con fines terapéuticos. No disponemos, sin embargo, de ninguna prueba funcional que tenga valor clínico para exponer esta importante función hepática.

Eppinger, refiriéndose a la prueba de Quick sobre la síntesis del Acido Hipúrico nos dice: "Considerando los trabajos dedicados a este asunto se tiene la impresión de que este problema (la exploración funcional antitóxico) se ha menospreciado. Quizas se deba a que las molestias de los análisis no compensen en modo alguno los resultados obtenidos con esta prueba."

En el curso de una investigación sobre cirrosis experimental en perros (2, 3) hemos comprobado la sensibilidad antitóxica hepática. La dosis de pentotal sódico, para cuatro horas de anestesia es de 300 mlgs. El hígado lesionado necesita la mitad, y más lesionado la 1/4 parte y aún, con esa pequeña cantidad duermen 24 horas. En el presente trabajo hemos utilizado ocho perros de peso que oscilaba entre 24 a 33 libras. Les inyectamos intravenosamente 0.45 mlgr. fenobarbital sódico señalado con C14. Los animales normales eliminaban en la orina de las 48 horas siguientes entre el 84.65 por ciento y el 95 por ciento de la dosis inyectada. Los recuentos en 3 ml. de suero de ocho animales a las 48 horas oscilaban entre 48 cts. a 170 cts. por minuto. Los mismos animales después de diferentes dosis de Tioacetamida eliminaron en la orina el: 29 por ciento, 29.9 por ciento, 30.9 por ciento, 31.18 por ciento, 56 por ciento, 67 por ciento, 74.51 por ciento y 86 por ciento.

Los contajes en 3 mlg. de sangre de estos animales a las 48 horas oscilaron entre 201 cts. y 4.300 cts. por minuto (Cuadro 1).

Del Centro Nuclear y Hospital Oncológico.

En el curso del experimento hemos tomado biopsias por aguja del hígado de los animales. La histopatología de las biopsias demuestra que en las necrosis fatales ocurrió el máximo de retención de Pentotal sódico C14 en sangre y el mínimo de eliminación del Pentotal sódico C14 en orina a las 48 horas. Los hígados, menos afectados histopatológicamente correspondían a los animales que eliminaron mayor cantidad de Pentotal sódico C14 en orina y retuvieron el mínimo en la sangre a las 48 horas (Figs. 2, 3, 4).

Se sabe que los hipnóticos de acción muy rápida y fugas son inactivados por hepáticos y eliminados

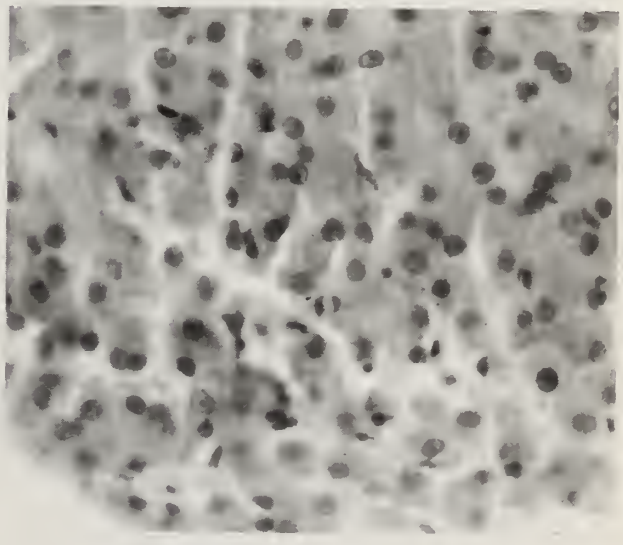


Fig. 1: *Biopsia de hígado tomada con aguja del ejemplar 1 Bis que demuestra la etapa temprana de la intoxicación con tioacetamida. Se nota discreta distorsión de los cordones celulares, algún edema intersticial y muy leves alteraciones nucleares. X 400. Tinción con H. E. CTS en orina - 86 por ciento - CTS en suero - 559 cts.*

GRAFICA 1
INYECCION PENTOBARBITAL C-14 INTRAVENOSA

	PERROS NORMALES			PERROS DESPUES DE ADMINISTRARLES 500 MLGR. DE THIOACETAMIDA	
Ejemplares No.	Contaje en Orina 24 Horas Después de Inyección (Por Ciento)	Contaje en Sangre 24 Horas Después de Inyección (CTS)	Ejemplares Bis	Contaje en Orina 24 Horas Después de Inyección (Por Ciento)	Contaje en Sangre 24 Horas Después de Inyección (CTS)
1	95,00	56	1	74,55 (Fig. 1)	201
2	86,00	559	2	67,00	2459
3	94,00	81	3	56,00 (Fig. 2)	4300
4	84,00	94	4	49,00	753
5	91,00	67	5	29,00 (Fig. 3)	502
6	85,60	170	6	29,90	551
7	92,08	116	7	30,90	572
8	93,50	68	8	31,18	559

GRAFICA 2
INYECCION 250 MLG. BENZOATOSODICO C14 INTRAVENOSO EN 3.5 cc AGUA DESTILADA

Ejemplares No.	PERROS NORMALES Contaje en Orina 24 Horas Después de Inyección (Por Ciento)	Ejemplares Bis	Contaje en Orina 24 Horas Después de Inyección (Por Ciento)
1	58,3	1	26,0
2	62,0	2	29,0
3	57,6	3	44,5

250 Mg. INTRAVENOUS INJECTION OF ^{14}C-SODIUM BENZOATE IN 3.5 cc OF DISTILLED WATER

Sample No.	NORMAL DOGS Urine Count 24 Hours After Injection (Percent)	Sample Bis	Urine Count 24 Hours After Injection (Percent)
1	58,3	1	26,0
2	62,0	2	29,0
3	57,6	3	44,5

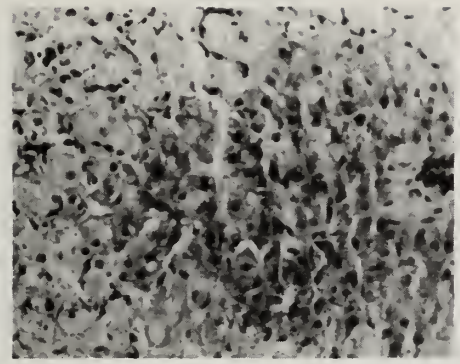


Fig. 2: *Ejemplar 3 Bis. Intoxicación con tioacetamida en etapa avanzada. Nótese la marcada distorsión de los cordones de hepatocitos. Las alteraciones van desde la degeneración hidrópica del citoplasma a la necrosis celular con alteraciones nucleares diversas. El tejido intersticial es edematoso y demuestra discreta reacción leucocitaria. Tinción H. E. X250. CTS en orina - 67 por ciento - CTS en suero - 2.496.*

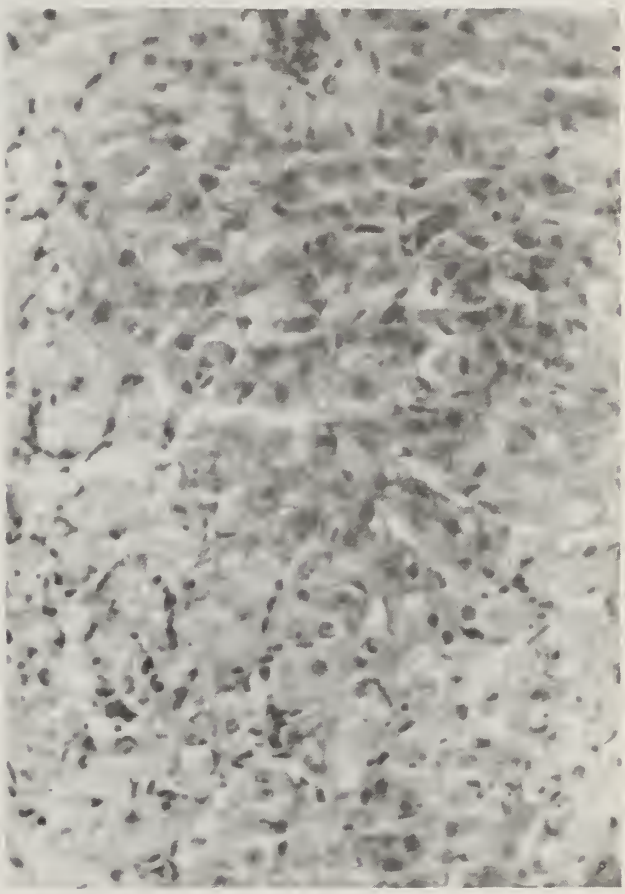


Fig. 3: *Ejemplar 5 Bis. Caso de intoxicación severa con tioacetamida. Se observa extensa necrosis de las células hepáticas con desaparición de la arquitectura del parenquina. La imagen es similar a la necrosis aguda. Tinción H. E. X 250. CTS en orina - 29 por ciento - CTS en suero - 4.300.*

por el riñón (4, 5).

En otra serie de experimentos hemos iniciado la investigación con radioisótopos, de la prueba de la función antitóxica hepática, con el Benzoato sódico señalado con C14. El Benzoato sódico es la base de la única prueba de la función antitóxica del hígado conocida como la prueba de Quick (6). A esta prueba se refería Eppinger al decir que "las molestias de los análisis no compensan los resultados obtenidos".

La facilidad y la precisión de las técnicas radioisotopas nos ha decidido a revisar este problema.

A una serie de perros normales de peso entre 10 a 15 libras les hemos inyectado intravenosamente en ayunas 250 de Benzoato sódico señalado C14 y disueltos en 3.5 de agua destilada. Se recogió la orina en jaulas especiales en las 24 horas siguientes. Después hemos adminstradoi a los mismos perros (bis) 500 de tioacetamida y a las 24 horas después repetíamos la inyección intravenosa de 250 de Benzoato sódico señalado con C14 disueltos en 3.5 c.c. de agua destilada. Se recogió la orina en las 24 horas siguientes.

La gráfica 2 evidencia los resultados obtenidos en 3 perros. Los resultados de la investigación con el Benzoato sódico señalado con C14 no han sido tan concluyentes como el Pentotal sódico.

No obstante haber evitado la posibilidad de mala absorción intestinal adoptando la técnica de la inyección intravenosa indicada por Quick por el mismo motivo, quizás la insuficiencia de glicina circulante para la síntesis del ácido hypúrico sea la causa de que solo apareció en la orina alrededor del 60 por ciento del Benzoato sódico inyectado.

Es lógico que la función antitóxica del hígado sea más rigurosa con los verdaderos tóxicos aunque entren en el cuerpo en dosis mínimas. Los resultados experimentales comunicados en este trabajo nos animan

a proseguir la investigación en trabajos con humanos usando como radioisotopos el Y 131.

Resumen

En una primera serie de ocho perros hemos investigado la eliminación urinaria de Pentobarbital sódico señalado con C14.

En los animales normales la eliminación en la orina a las 18 horas de la inyección de Pentobarbital C14 oscilaba entre el 84.65 por ciento y el 95 por ciento de la dosis inyectados. Los cómputos con sangre después de 24 horas oscilaron entre 48 cts. y 170 cts. por minuto por 3 ml.

Los mismos animales despnés de recibir diversas dosid del tóxico hepático eliminaron en orina un promedio de 55.27 por ciento oscilando entre 29 por ciento y 86 por ciento. Los cómputos en sangre oscilaron entre 4.300 cts. y 201 cts. por minuto por 3 ml.

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EL MERCADO DE LOS SERVICIOS MEDICOS

Annette B. Ramírez de Arellano, MCP, MCHP

La crisis en los servicios de salud usualmente se define como la creciente brecha entre la demanda por estos servicios y los recursos disponibles para satisfacerla. Debido a que la demanda por los servicios se toma como dada — algo no susceptible a reducción — la solución que más frecuentemente se propone para cerrar la brecha es: más recursos. Esto a su vez suele traducirse en una recomendación más específica: más médicos.

Desafortunadamente, esta receta parte de un diagnóstico erróneo de cómo opera el mercado de servicios médicos. Es por eso necesario aclarar cuál es la dinámica de ese mercado, y corregir algunas de las falacias que se sostienen al respecto.

La exposición a continuación consta de dos partes. En primer lugar se examinan las características económicas particulares del cuidado médico, recalcando cómo éste difiere de los demás bienes y servicios que se obtienen en el mercado. La segunda sección intenta refutar una serie de ideas equivocadas frecuentemente utilizadas para justificar un aumento en el número de médicos. En cada caso, se presenta evidencia empírica y teórica de una variedad de fuentes.

I. Características Distintivas del Servicio Médico

En economía la existencia de un mercado competitivo modelo se basa en una serie de supuestos: (1) que hay una multiplicidad de compradores y vendedores bien informados, ninguno de los cuales es suficientemente poderoso para controlar los precios; (2) que no hay colusión ni entre los compradores ni entre los vendedores; y (3) que hay libertad de entrada para compradores y vendedores que no están actualmente en el mercado (1). Un análisis de los servicios médicos revela cuán poco se ajustan éstos a los supuestos de un mercado de libre competencia, como se indica a continuación (2).

Escasez relativa de vendedores:

Aun en la mayor parte de las áreas urbanas el mercado es demasiado limitado para justificar suficientes médicos en cada categoría para cumplir con los requisitos de un mercado competitivo. Además, las asociaciones profesionales ejercen presiones indirectas para mantener los honorarios médicos por encima de un mínimo aceptable, creando así una situación de colusión (3).

Falta de información:

El modelo de mercado económico clásico asume un consumidor soberano que, al decidir si comprar o no, qué comprar, cuándo y dónde, controla su actividad económica. Sin embargo, la naturaleza de la salud y la enfermedad limitan en gran medida la soberanía del consumidor de servicios de salud. Al ser la enfermedad involuntaria e impredecible, la capacidad del consumidor para decidir qué servicio obtener se limita seriamente. Debido a que en un momento dado es imposible determinar qué tipo de servicio es necesario, el lego actúa sobre presunción de necesidad. En otras palabras, la única manera del paciente saber si necesita ir o no a un médico es yendo al médico.

Una vez el paciente decide acudir al médico, es éste quien decide qué clases de servicios se requieren, y con qué frecuencia. También es el médico quien receta los demás bienes y servicios que necesita el paciente, tales como drogas y hospitalización. Aun sin ser un empleado del hospital, el médico en gran medida determina lo que ocurre en la institución:

Es él quien decide quién entra, qué se le hace al

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paciente mientras está hospitalizado, y cuánto ha de permanecer allí. Es el médico quien, en gran medida, controla las actividades de las enfermeras y de los técnicos, quienes le rinden informes y siguen sus instrucciones....(4)

El consumidor también se ve impedido de actuar racionalmente debido a que no tiene los conocimientos sobre la calidad técnica y el precio del servicio que le permitirán seleccionar entre diversas alternativas. Los anuncios competitivos y las "guerras de precios" no sólo no se fomentan en los servicios médicos sino que se consideran poco éticos y reprochables (5).

Límites a la libre entrada:

Las leyes de licenciatura impiden el que haya una entrada libre al mercado de servicios de salud. Aunque este tipo de mecanismo suele justificarse como medida para proteger al público contra el proveedor incompetente, también actúa como una barrera al mercado, situación que hace inaplicable el último postulado de un mercado competitivo.

II. Falacias en Torno a los Servicios Médicos

Como se ha señalado anteriormente, el cuidado médico se desvía significativamente del comportamiento económico usual de otros servicios que se ofrecen en un mercado.

En el modelo clásico de un mercado, la oferta y la demanda surgen separadamente y se mantienen en equilibrio mediante el movimiento en los precios. Un aumento en la oferta relativo a la demanda ocasiona una baja en los precios. Esto a su vez propende un aumento en la demanda. Este mecanismo de ajuste no ocurre en el mercado de los servicios de salud. Como señala Eli Ginzberg, en este sector "el control sobre la expansión (del consumo)....lo determina principalmente la disponibilidad de la oferta. En resumen, ¡la oferta de los recursos médicos en efecto genera su propia demanda! "(6). Es a la luz de este fenómeno que deben analizarse las aseveraciones que se hacen con relación a los recursos médicos.

Falacia Núm. 1: Un aumento en el número de médicos reduce el costo de los servicios.

Esta alegación asume que, cuando aumenta la oferta de un servicio, se reduce el costo unitario del mismo. Las particularidades de los servicios médicos hacen que éstos operen a la inversa de los demás bienes y servicios. Como señala Reinhardt:

> El primer rasgo distintivo del mercado de servicios médicos radica en que la demanda no es independiente de la oferta. El segundo es que los médicos probablemente tienen amplia discreción en establecer el precio de sus servicios; hay evidencia de que, dentro de un amplio margen, los médicos pueden fijar sus honorarios para lograr un nivel de ingresos deseado. Dadas estas características del mercado, es probable que un exceso de médicos genere un *aumento* en vez de una reducción en los costos de los servicios de salud (7).

Debido a que los médicos controlan en gran medida la demanda por sus propios servicios — así como la de otros bienes y servicios ancilares — las consecuencias inflacionarias de exceso de médicos tienen un efecto multiplicador. El alza en costos tiende a manifestarse en el largo plazo:

> Entretanto, es probable que el exceso permanezca camuflado por ineficiencias en la producción de una mejor salud (mediante la prestación y prescripción de servicios innecesarios) o por ineficiencia en la producción de servicios de salud (mediante una mala utilización del tiempo del médico). Cualquiera de los dos tipos de ineficiencia aumentará el costo de los servicios, y que ese costo será, por supuesto, sufragado por los pacientes o por los que indirectamente pagan por ellos (8).

Es en vista de esta situación que Marc Lalonde, el Ministro de Salud del Canadá, ha propuesto medidas estrictas para controlar el número de médicos dentro del país, considerando que éstos son excesivos (9).

Además del efecto inflacionario — que es precisamente lo contrario a lo que se pretende lograr mediante un aumento en los recursos médicos — la posibilidad de una proliferación de servicios innecesarios no debe pasarse por alto. La creciente evidencia de cirugía innecesaria y contraindicada es suficiente para re-evaluar la cantidad y calidad de los servicios médicos (10).

Si no se puede depender del mercado para producir los servicios de salud que se requieren, tampoco se puede depender del mercado para distribuirlos de acuerdo a las necesidades de la población. Es por lo tanto necesario refutar la segunda falacia en cuanto a los servicios médicos.

Falacia Núm. 2: Un aumento en el número de médicos resulta en una mejor distribución geográfica de este personal.

La estrategia de aumentar el número de médicos como manera de lograr una mejor distribución de los recursos asume que el exceso de médicos en áreas con servicios adecuados se redistribuirá, ubicándose en áreas subservidas. Esto a su vez parte de la premisa de que son los consumidores, en vez de los proveedores, los que determinan la distribución de los recursos de salud.

La evidencia disponible refuta la validez de esta estrategia; como indica Rashi Fein, "producir médicos porque Harlem no tiene suficientes servicios no va a traer esos médicos ni sus servicios a Harlem" (11).

En Puerto Rico, el número de médicos aumentó de 80 a 120 por cada 100,000 habitantes entre 1958 y 1972, pero las disparidades geográficas no se nivelaron durante este período (12). Datos para 1972 indican que mientras la Región Noreste, que incluye el área metropolitana de San Juan y los municipios limítrofes, tenía aproximadamente 185 médicos por 100,000 habitantes, y la Región Norte, que era la peor dotada, tenía solo 61 (13).

Los datos sobre la distribución de médicos en los Estados Unidos indican que la mala distribución se ha agudizado tanto en términos geográficos como funcionales a medida que ha aumentado el personal. La concentración de personal médico se ha acentuado en áreas urbanas de mayor población y en las secciones de mayores ingresos dentro de las áreas metropolitanas (14). Es por esta situación que Tudor Hart ha postulado el "inverse care law" que opera en el sector salud: la disponibilidad de buenos servicios médicos tiende a mostrar una relación inversa con las necesidades de la población servida (15).

La estrategia de "inundar" el mercado de servicios de salud no solo no resolvería el problema de la mala distribución, sino que resultaría altamente costosa. Como concluye Fein: "No se puede responsablemente abogar por una política para resolver el desequilibrio del mercado (de los servicios médicos) aumentando la oferta que mediante un proceso de filtración o sobreabundancia, las áreas más pobres estén servidas. Los costos de producir esos recursos humanos adicionales, así como los costos de prestar un exceso de servicios ("overdoctoring") en las áreas que tendrían una mayor oferta de servicios que los que tienen en la actualidad, nos impiden recomendar esa solución" (16).

Falacia Núm. 3: En el largo plazo, un aumento en el número de médicos reduce la demanda por servicios de salud.

Esta tésis parte del supuesto de que un aumento en el número de médicos disponibles reducirá el reservorio de necesidades médicas y, consecuentemente, la demanda por servicios de salud. Sin embargo, como señaláramos anteriormente, en los servicios médicos opera una "Ley de Parkinson" que resulta en que la demanda por estos servicios es prácticamente ilimitada y, por lo tanto, insaciable (18). Esto se ha debido principalmente a dos fenómenos relacionados: 1) una tendencia de parte del público de acudir al médico para condiciones más leves; y 2) una redefinición de lo que son servicios de salud.

Paradójicamente, el primero de estos fenómenos ha sido el resultado de las mejoras registradas en las condiciones de salud de la población. Síntomas que anteriormente se consideraban transitorios o triviales, ahora se consideran meritorios de atención médica:

> Ahora que la probabilidad de la muerte prematura se ha reducido y muchas de las condiciones severas e incapacitantes se han controlado, los individuos han comenzado a prestarle mayor atención a las enfermedades y malestares menores. Ahora perciben y actúan en base a síntomas que anteriormente hubiesen ignorado.... El resultado es que, mientras la salud de la población ha mejorado en términos absolutos, el público está solicitando y recibiendo muchos más servicios médicos (19).

Debido a que las expectativas del público han aumentado y la aceptación del dolor y el malestar ha bajado, una mejor salud no ha sido acompañada por una reducción en la demanda por servicios de salud.

Paralelo a este fenómeno, y en parte como consecuencia de él, ha habido un cambio significativo en la naturaleza y el ámbito de los servicios de salud:

> El cambio en los tipos de morbilidad que requieren tratamiento médico no ha sido meramente cuantitativo. También ha ocurrido un cambio cualitativo. Los pacientes le están prestando a los médicos un tipo de morbilidad completamente nuevo, y el bregar con estas nuevas demandas requiere una nueva estrategia en la prestación de los servicios de salud (20).

Varios autores (21) también han señalado que pro-

blemas que anteriormente se consideraban morales, legales o sociales y se resolvían a través de la iglesia, los tribunales o los servicios de bienestar, respectivamente, ahora se manifiestan en el sector médico, donde se espera encontrarles solución. La lista de problemas que se han redefinido como "issues" médicos incluye el alcoholismo, la adicción a drogas, el crimen, la discordia matrimonial, desviaciones en el comportamiento, y el control de la fecundidad.

En resumen, vemos que el utilizar un aumento en el número de los recursos médicos para controlar los costos resulta contraproducente, y que el uso de esta estrategia para lograr una distribución más equitativa de los servicios y reducir la demanda por servicios resulta ilusorio.

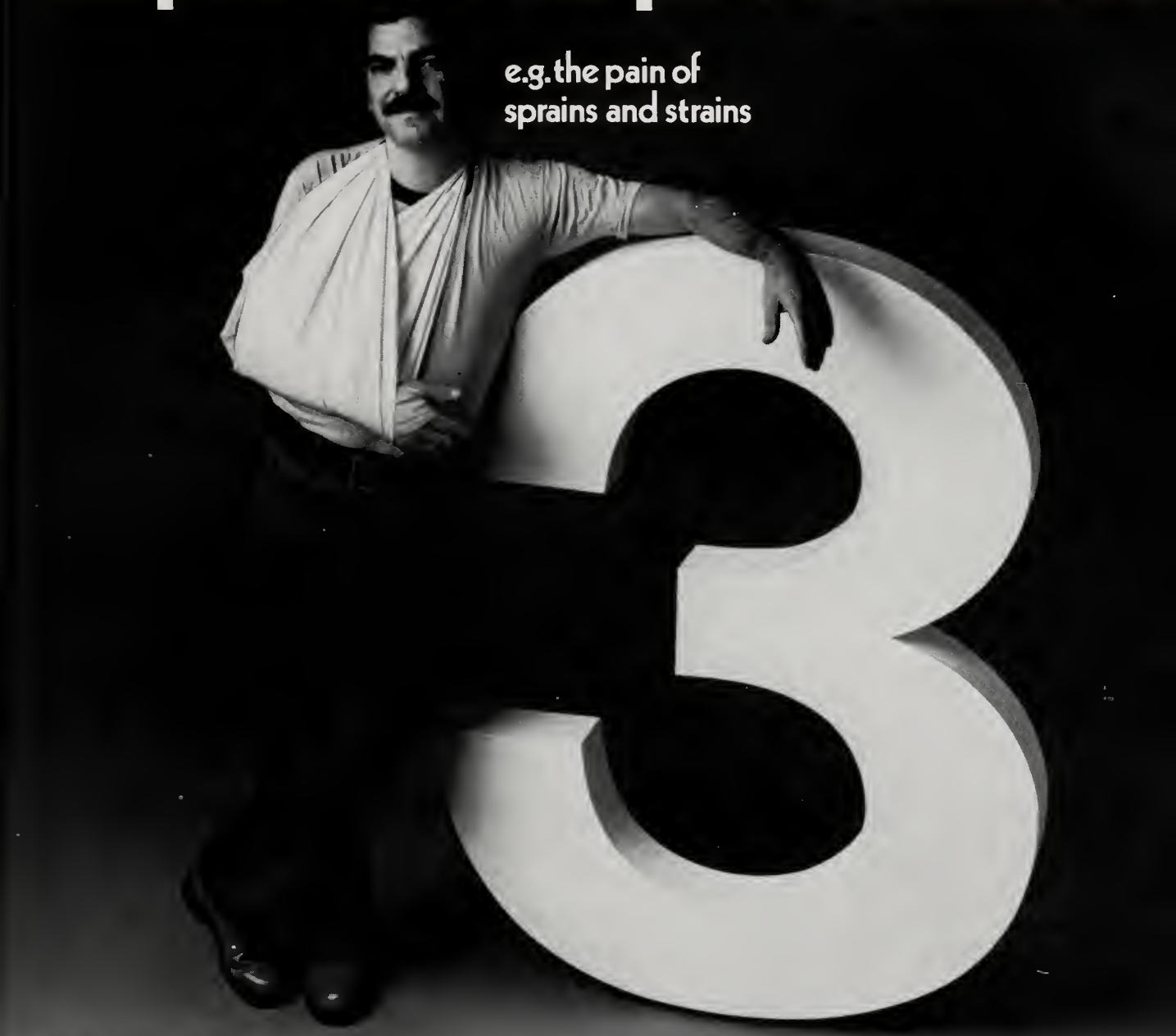
Summary

The health care crisis is usually defined as the increasing gap between the supply of services and the demands of the consuming public. An increase in the number of physicians is usually proposed as the means by which the gap may be reduced. This article examines the validity and limitations of this strategy. The first part describes the peculiarities of medical care, pointing out the various ways in which the market for health services differs from that for other goods and services. The second part examines and refutes the commonly held beliefs that an increase in the number of physicians will reduce costs, bring about a more equitable distribution of care, and reduce the demand for services.

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Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or

New Septra® DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Double Strength tablet dosage: 1 tab b.i.d.



jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **At present, data are insufficient to recommend use in infants and children under 12.**

Precautions: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

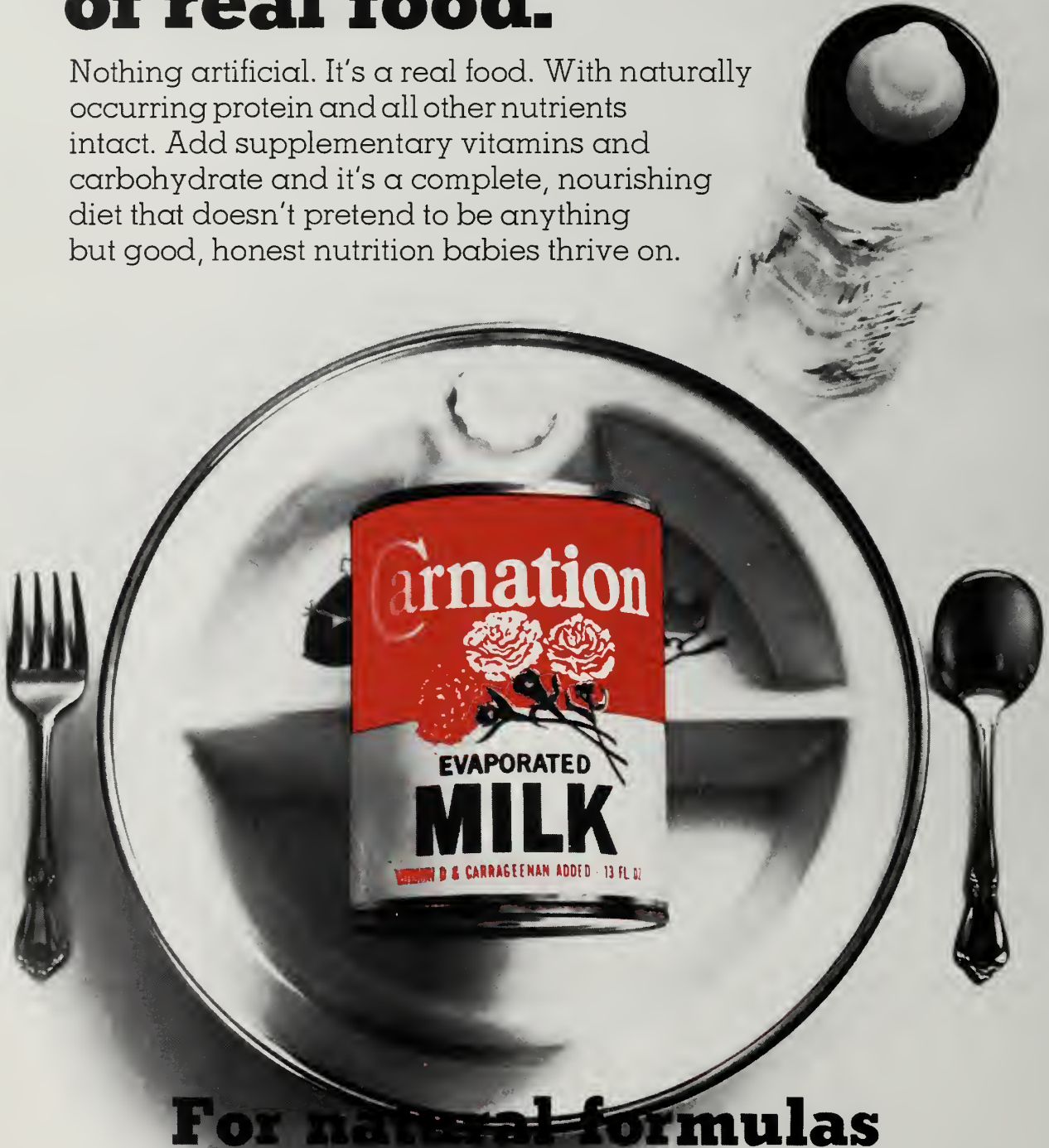
Supplied: Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Carnation Evaporated Milk. Baby's first taste of real food.

Nothing artificial. It's a real food. With naturally occurring protein and all other nutrients intact. Add supplementary vitamins and carbohydrate and it's a complete, nourishing diet that doesn't pretend to be anything but good, honest nutrition babies thrive on.



For natural formulas

CARNATION® EVAPORATED MILK. CARNATION COMPANY. LOS ANGELES. CALIF. 90036

A CRITICAL ASSESSMENT OF HEALTH CARE ECONOMY

One of the great outcries of the day is that privately oriented health care is not economical and systematic enough and that the federal government should spring to the rescue, a la Rin Tin Tin. But how deft is the government (notably the Social Security Administration) in cost management? How qualified is it to administer any program of National Health Insurance? How blameless is it for the expense of Medicare?

Negative answers can be inferred from a recently released study of Medicare Part A cost performance. What makes the study especially noteworthy is its source: the General Accounting Office (GAO), a federal agency.

GAO compared SSA's performance with that of four private insurance companies in dealing with institutional providers of Medicare services.

The average cost – excluding audit – of a bill processed by SSA's Division of Direct Reimbursement (DDR) was $12.39 in 1973, compared with $7.31 for Travelers, $7.28 for Mutual of Omaha, $3.81 for Blue Cross of Chicago, and $3.55 for Blue Cross of Maryland. The lower costs for the "Blues" were attributed partly to their smaller, more wieldly territories.

However, GAO found that "higher salaries and lower productivity appear to be major reasons for the higher costs of the Division (DDR), which, unlike the private intermediaries, had no production standards."

DDR's annual compensation exceeded that of neighboring Maryland Blue Cross by 25 percent for accountants and auditors, 51 percent for claims examiners.

"Despite DDR's higher costs," the report continued, "it generally took longer than other intermediaries to pay bills and settle with providers. Its error rate was average."

Adding to the weight of the findings is the nonpolitical, independent character of the General Accounting Office. It is the fiscal watchdog of Congress, though its head (the Comptroller-General) is appointed by the President. Its Medicare report was a detailed response to questions put to it by the House Ways and Means Committee chairman.

All of this should be borne in mind in weighing the rebuttals from the Department of Health, Education, and Welfare – and from Max W. Fine, executive director of the Committee for National Health Insurance and prolific writer of sly "letters to the editor" of newspapers.

HEW – and Fine – call the report outdated. But DDR's lack of cost data (GAO had to develop them) could help explain the delay.

HEW contends that its costs per bill are overstated for 1973 since bills processed through magnetic tape are excluded. HEW also maintains that costs have dropped since 1973, though this is also true for other carriers in the study. GAO said it has not verified the new figures.

So the burden of proof hangs heavy on the Social Security Administration. Meanwhile, Congress ought to think hard about the report from its fiscal watchdog. And think hard about making SSA the health-insurance administrator for the public at large, as proposed in such legislation as the Kennedy bill.

American Medical Association

LISTA DE ANUNCIANTES

1. BURROUGHS WELLCONE

   Empirin Comp. w/Codeine
   Septra

2. CARNATION COMPANY

   Evaporated Milk

3. EATON LAB.

   Furacin

4. ROCHE LAB.

   Azo Gantanol
   Librium
   Valium

5. ROERIG & CO.

   Antivert

6. W. H. RORER

   Ascriptin A/D

7. SMITH, KLINE & FRENCH

   Dyazide

8. SYNTEX LAB.

   Neo-Mull-Soy

9. UPJOHN CO.

   Medrol Dosepak

Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

Warnings: Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

Supplied: Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

When pain complicates acute cystitis*

Azo Gantanol®

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

for the pain for the pathogens



☐ **Early relief of painful symptoms** such as burning and discomfort associated with urgency and frequency.

☐ **Effective control of susceptible pathogens** such as *E. coli, Klebsiella-Aerobacter, Staph. aureus, Proteus mirabilis* and, less frequently, *Proteus vulgaris.*

☐ **Appropriate antibacterial therapy:** up to three days with Azo Gantanol, then 11 days with Gantanol® (sulfamethoxazole).

*nonobstructed; due to susceptible organisms

ROCHE

DYAZIDE®

Trademark

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

MAKES SENSE FOR LONG-TERM CONTROL OF HYPERTENSION*



Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* **Warning**
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F CO., Carolina, P.R. 00630
Subsidiary of SmithKline Corporation

TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE

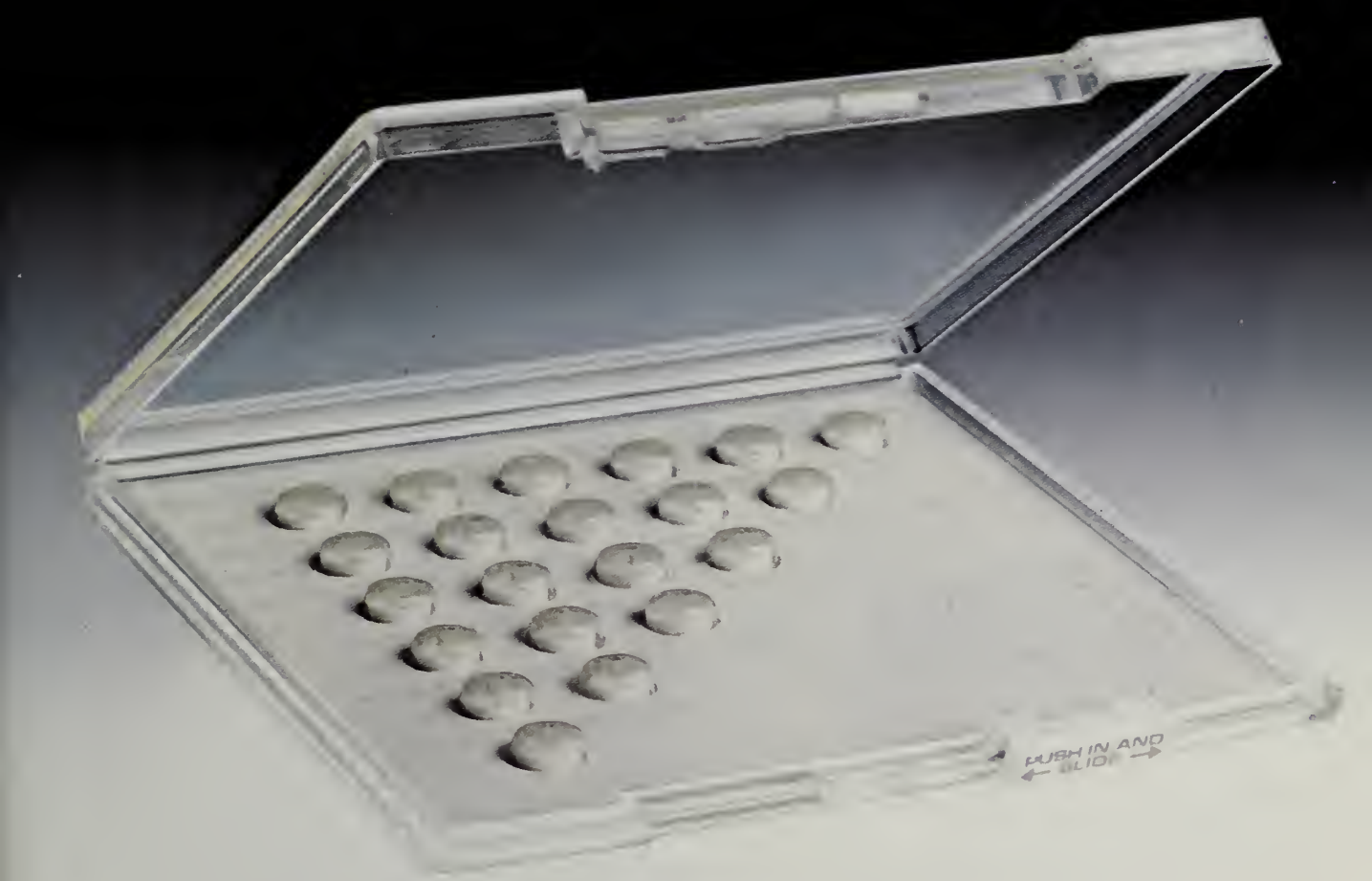
Upjohn

The Upjohn Company, Kalamazoo, Michigan 49001

Medrol® 4 mg Dosepak*

methylprednisolone, Upjohn

The explicit printed dosage instructions that accompany each Dosepak make it easy for the patient to understand and follow the dosage regimen.



*Trademark



When Big Ben looks "a little off"...

Antivert®/25
(meclizine HCl) 25 mg. Tablets
for vertigo*

▪ **Most Widely Prescribed**—Antivert is the most widely prescribed agent for the management of vertigo* associated with diseases affecting the vestibular system such as Menière's disease, labyrinthitis, and vestibular neuronitis.

▪ **Relief of Nausea and Vomiting**—Antivert/25 can relieve the nausea and vomiting often associated with vertigo.*

▪ **Dosage for Vertigo***—The usual adult dosage for Antivert/25 is one tablet t.i.d.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Para enmendar el Título y los Artículos 1, 2, los incisos (a) y (d) del Artículo 3 y adicionar el inciso (e) a dicho artículo; y enmendar los Artículos 4, 5, 6, 8, 9, 11, 12 y 14 de la Ley núm. 26 de 13 de noviembre de 1975, conocida como "Ley de la Administración de Facilidades y Servicios Hospitalarios de Salud de Puerto Rico".

Decrétase por la Asamblea Legislativa de Puerto Rico:

Sección 1.—Se enmienda el título de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"LEY

Para crear la Administración de Facilidades y Servicios de Salud de Puerto Rico, adscrita al Consejo General de Salud; definir sus propósitos, poderes, deberes, responsabilidades, organización y funcionamiento; transferir a esta Administración las facilidades y servicios de salud que actualmente administra y opera el Departamento de Salud; conferir poderes a las agencias estatales, subdivisiones políticas e instrumentalidades del Estado Libre Asociado para entrar en convenios con la Administración para la adquisición, la administración y operación de facilidades de salud."

Sección 2.—Se enmienda el Artículo 1 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 1.—Propósitos Legislativos

Es el propósito de esta ley, fomentar una administración y operación de facilidades y servicios de salud de alta eficiencia y eficacia, con la flexibilidad necesaria que propenda a la integración y coordinación de servicios de salud accesibles para todo el Pueblo de Puerto Rico, que es la responsabilidad constitucional e ineludible de cualquier gobierno responsable. Para lograr tales fines, se crea la Administración de Facilidades y Servicios de Salud de Puerto Rico.

Dicha Administración tendrá los poderes necesarios para administrar y operar las facilidades para la protección y el cuidado de la salud que actualmente administra y opera el Departamento de Salud del Estado Libre Asociado de Puerto Rico, así como las facilidades hospitalarias de salud que pueda adquirir en el futuro."

Sección 3.—Se enmienda el Artículo 2 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 2.—Título Breve

Esta ley se conocerá como 'Ley de la Administración de Facilidades y Servicios de Salud de Puerto Rico'."

Sección 4.—Se enmiendan los incisos (a) y (d) y se adiciona el inciso (e) al Artículo 3 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 3.—Definiciones

Las siguientes frases y términos tendrán los significados que se indican a continuación cuando sean usados o se haga referencia a los mismos en esta ley, a no ser que el contexto claramente indique otra cosa:

(a) 'Administración' significará la Administración de Facilidades y Servicios de Salud de Puerto Rico, establecida por esta ley.

(b) .....

(c) .....

(d) 'Consejo' significará el Consejo General de Salud creado por la 'Ley de Reforma Integral de los Servicios de Salud de Puerto Rico'.

(e) 'Comité Ejecutivo' significa el Comité Ejecutivo de los Servicios de Salud del Consejo, creado por la 'Ley de Reforma Integral de los Servicios de Salud de Puerto Rico'."

Sección 5.—Se enmienda el Artículo 4 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 4.—Creación de la Administración de Facilidades y Servicios de Salud de Puerto Rico.

(a) Se crea la Administración de Facilidades y Servicios de Salud del Estado Libre Asociado de Puerto Rico, adscrita al Consejo General de Salud. Las funciones de esta Administración constituirán un servicio esencial de carácter público, conforme a la política pública que emana de la legislación vigente en relación con los servicios de salud del Estado.

(b) Los poderes de la Administración se ejercerán por el Consejo, a través del Comité Ejecutivo de dicho Consejo. Dicho Comité Ejecutivo actuará como la Junta de Gobierno de la Administración.

(c) La Administración tendrá un Director Ejecutivo nombrado por el Comité Ejecutivo con la aprobación del Consejo.

El Director Ejecutivo será el primer ejecutivo de la Administración; la representará en todos los actos y en los contratos que fuere necesario otorgar en el ejercicio de sus funciones; y desempeñará los deberes y tendrá las responsabilidades, facultades y autoridad que le sean delegadas por el Consejo. El sueldo del Director Ejecutivo será fijado por el Consejo, pero nunca será mayor que el sueldo del Secretario de Salud.

El Director Ejecutivo desempeñará su cargo a voluntad del Consejo.

(d) El Consejo podrá delegar en el Director Ejecutivo o en otros empleados de la Administración cualquiera de sus poderes, excepto el poder de reglamentación.

Sección 6.—Se enmienda el Artículo 5 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 5.—Poderes Generales

La Administración tendrá todos los poderes necesarios y convenientes para llevar a cabo y efectuar los propósitos y las disposiciones de esta ley; incluyendo, pero sin que se entienda como una limitación, los poderes para:

(a) Adoptar, alterar y usar un sello del cual se tomará conocimiento judicial;

(b) Mantener una oficina en la Capital del Estado Libre Asociado de Puerto Rico y en cualquier otro lugar que estime necesario;

(c) Formular, adoptar, enmendar y derogar reglas y reglamentos necesarios para la operación y funcionamiento interno de la Administración;

(d) Administrar y operar las facilidades de salud que actualmente administra y opera el Departamento de Salud y las que pueda adquirir en el futuro;

(e) Contratar servicios profesionales y de consulta previa aprobación del Consejo a través de su Comité Ejecutivo.

(f) Contratar o de cualquier otra forma convenir con organismos públicos o privados, denominados en esta ley 'entidades participantes', para ofrecer servicios administrativos y técnicos que permitan agilizar las operaciones de sus facilidades;

(g) Hacer disponible, por medio de contrato, a la Universidad de Puerto Rico las facilidades necesarias en las facilidades gubernamentales de servicio de salud para llevar a cabo las fases prácticas de la educación y de profesionales de la salud;

(h) Establecer su propia estructura administrativa y establecer, organizar y administrar sus propios sistemas de personal, presupuesto, contabilidad, compras y suministro y cualesquiera otros sistemas administrativos necesarios para una operación eficiente y económica, sin sujeción a la Ley de Compras y Suministros del Estado Libre Asociado de Puerto Rico ni a las reglas y reglamentos promulgados al amparo de dicha ley.

El personal de la Administración quedará comprendido en el Servicio Exento, a tenor con las disposiciones de la Ley núm. 5 de 14 de octubre de 1975. La administración de personal de la Administración estará basada en el principio de mérito. Las normas y reglamentos que adopte la Administración para la administración de personal se harán en coordinación y con el asesoramiento de la Oficina Central de Administración de Personal del Estado Libre Asociado de Puerto Rico.

Los funcionarios y empleados de cualquier organismo, dependencia o instrumentalidad del Estado Libre Asociado de Puerto Rico y de los Gobiernos Municipales que sean nombrados por la Administración y que al momento del nombramiento fueren beneficiarios de cualquier sistema o sistemas existentes de pensión, retiro o de fondos de ahorro y préstamo continuarán teniendo después de dicho nombramiento los derechos, privilegios, obligaciones y status, respecto a los mismos, que la ley prescribe para los funcionarios y empleados que ocupan puestos similares en el Gobierno del Estado Libre Asociado.

Todos los demás funcionarios y empleados nombrados para puestos en la Administración no comprendidos en la categoría descrita en el párrafo anterior, tendrán los derechos, privilegios, obligaciones y status respecto a convertirse en beneficiarios de cualquier sistema o sistemas existentes de pensión, retiro o de fondo de ahorro y préstamo, como si hubiesen sido nombrados para un tal puesto similar en el Gobierno del Estado Libre Asociado de Puerto Rico.

Se garantiza a todos los empleados que prestan servicios en los programas del Departamento de Salud y que sean transferidos a la Administración que se crea mediante esta ley y que fueron nombrados en virtud de la Ley núm. 345 de 12 de mayo de 1947, según enmendada, conocida como Ley de Personal. los derechos adquiridos bajo la ley antes mencionada y de otras leyes aplicables, así como los derechos, privilegios y obligaciones y status respecto a cualquier sistema, o sistemas existentes de pensión, retiro o fondo de ahorro y préstamo al cual estuvieren afiliados.

En adición se garantizan los derechos adquiridos en virtud de cualquier contrato o acuerdo de cualesquiera otros empleados que sean transferidos a la Administración, conforme al Artículo 8 de esta ley.

El sistema de compras y suministro que se establezca, proveerá para la celebración previa de subastas, excepto cuando el gasto a incurrirse no exceda de cinco mil (5,000) dólares. Disponiéndose, que en caso de emergencia declarada por el Gobernador del Estado Libre Asociado de Puerto Rico, la Administración podrá comprar sin sujeción a subasta, conforme a la aprobación del Gobernador en estos casos. El mismo suplirá a la Administración y a las entidades participantes que así lo convengan con la Administración, todos aquellos materiales, suministros, equipos, piezas y servicios que sean necesarios para la prestación de servicios de salud.

(i) Adquirir mediante donación o por arrendamiento cualquier propiedad mueble o inmueble, mejorada o sin mejorar, y derechos sobre terrenos;

(j) Negociar y otorgar toda clase de contratos y otros instrumentos públicos con personas, firmas, corporaciones, agencias gubernamentales y otras entidades para lograr los propósitos de esta ley conforme a la Ley 213 de mayo de 1948, según enmendada, y la Ley 56 del 21 de julio de 1969, según enmendada. Los municipios, departamentos, divisiones, agencias e instrumentalidades del Estado Libre Asociado de Puerto Rico, están por la presente autorizados a concertar contratos y de cualquier otra forma cooperar con la Administración para facilitar el financiamiento, adquisición, operación o mantenimiento de cualquier facilidad;

(k) Fijar y recibir ingresos por el uso de sus facilidades y por la prestación de servicios y aplicar todo o parte del producto de dichos ingresos al pago de sus deudas, incluyendo rentas por el uso de sus facilidades siempre que ello no afecte su función principal de prestar servicios de salud;

(l) Gestionar el cobro y recobro de todas aquellas cantidades que le correspondan bajo los términos de cualquier ley federal o del Estado Libre Asociado de Puerto Rico;

(m) Tener control y supervisión sobre la naturaleza y necesidad de todos sus gastos y la forma en que los mismos han de incurrirse, autorizarse y pagarse, previa reglamentación que deberá ser aprobada por el Secretario de Hacienda;

(n) Tomar dinero a préstamo y garantizar el pago de sus deudas con los ingresos que genere de sus propias operaciones;

(o) Establecer y mantener una debida coordinación con el Comité Ejecutivo y cualquier agencia, subdivisión política o instrumentalidad pública relacionada con la prestación de servicios de salud."

Sección 7.—Se enmienda el Artículo 6 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 6.—Funciones de la Administración

La Administración será el organismo que administrará y operará las facilidades de salud que actualmente administra el Departamento de Salud y su función principal será la prestación de servicios de salud de acuerdo a las normas que establece esta ley, los reglamentos que se promulguen en virtud de la misma o que el Consejo establezca. Además tendrá las siguientes funciones y responsabilidades:

(a) Cuando Previa autorización del Consejo y cuando los recursos lo permitan establecerá un sistema de emergencia médica que cuente con un servicio de comunicación central coordinado, un sistema de transportación debida equipado y atendido con personal preparado y una red de salas de emergencia categorizadas por servicios y regiones;

(b) Cuando los recursos lo permitan y dentro del menor tiempo posible, establecerá clínicas multifásicas automatizadas que servirán para fomentar el diagnóstico temprano y el mantenimiento de la salud;

(c) Establecerá un moderno sistema de contabilidad que deberá incluir contabilidad de costo y utilización de servicios, en consulta con el Comité Ejecutivo.

(d) Contratará con la Organización de Revisión de Patrones de Servicios Profesionales (P. S. R. O.) de Puerto Rico para la revisión y evaluación de los servicios profesionales que se presten en las facilidades de salud administradas y operadas por la Administración;

(e) Establecerá una unidad de investigación sobre métodos modernos para la prestación de servicios de salud que aumenten la eficiencia y calidad de dichos servicios."

Sección 8.—Se enmienda el Artículo 8 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

"Artículo 8.—Operación por la Administración

La Administración queda autorizada para retener u obtener, mediante donación o por arrendamiento, la posesión de cualesquiera facilidades de salud, y para operar y mantener las mismas o hacer que éstas sean operadas y mantenidas bajo aquellos acuerdos que la Administración estime necesarios para lograr los propósitos de esta ley. A tales fines, dichas facilidades podrán ser operadas y mantenidas en unidades separadas o múltiples, bien por el propio personal de la Administración o por operadores y administradores independientes, bajo contrato, en cuyas cláusulas se proveerá, entre otras cosas, para el pago de una compensación en la forma y cantidad que la administración, separada o conjuntamente con los operadores y administradores independientes, determine que es razonable."

Sección 9.—Se enmienda el Artículo 9 de la Ley núm. 26 de 13 de noviembre de 1975, para que lea como sigue:

Artículo 9.—Transferencias

(a) Se transfieren a la Administración de Servicios y Facilidades de Salud las funciones y facultades del Secretario o Departamento de Salud contenidas en las siguientes disposiciones legales:

1) Artículos 1 y 2 de la Ley núm. 76 de 10 de mayo de 1937, según enmendada.
2) Ley núm. 107 de 5 de junio de 1973, según enmendada.
3) Ley núm. 142 de 7 de mayo de 1938, según enmendada.
4) Ley núm. 213 de 15 de mayo de 1948, según enmendada.
5) Ley núm. 44 de 17 de mayo de 1955.
6) Artículos 1 y 2 de la Ley núm. 36 de 12 de junio de 1961.

(b) Se autoriza y ordena al Secretario a transferir a la Administración el personal, records, equipo, materiales, fondos disponibles y el uso de las facilidades de salud que estén siendo o puedan ser utilizados en la prestación de servicios médicos-hospitalarios o que puedan estar siendo usados en relación con las leyes relacionadas anteriormente.

(c) Asimismo, se autoriza y se ordena al Secretario de Transportación y Obras Públicas para que previa aprobación del Consejo, traspase a la Administración el uso de los terrenos y estructuras propiedad del Estado Libre Asociado de Puerto Rico actualmente dedicadas por el Departamento de Salud a la prestación y el cuidado de la salud, excepto aquellas facilidades cuya construcción hayan sido financiadas por la Autoridad de Edificios Públicos o que están en proceso de ser adquiridas por ésta.

(d) Se faculta al Consejo para que delegue en la Administración cualquiera de los poderes y funciones que le confiere la Ley núm. 56 del 21 de julio de 1969, según enmendada.

Sección 10.—Se enmienda el Artículo 11 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

Artículo 11.—Todos los dineros de la Administración se ingresarán al Fondo de Salud. Las cuentas se harán de acuerdo con las normas y reglamentos prescritos por la Administración con la aprobación del Secretario de Hacienda.

Sección 11.—Se enmienda el Artículo 12 de la Ley núm. 26 de 13 de noviembre de 1975 para que lea como sigue:

Artículo 12.—La Administración establecerá con la aprobación del Secretario de Hacienda y el Consejo el sistema de contabilidad que se requiera para el adecuado control y registro de todas sus operaciones. Las cuentas de la Administración se llevarán de forma que puedan segregarse por actividades.

Sección 12.—Se enmienda el Artículo 14 de la Ley núm. 26 del 13 de noviembre de 1975, para que lea como sigue:

Artículo 14.—Informes.—La Administración someterá a la Legislatura y al Gobernador del Estado Libre Asociado de Puerto Rico, por conducto del Consejo y dentro de los noventa (90) días siguientes al cierre de cada Año Fiscal, los siguientes informes:

(a) Un estado financiero y un informe completo sobre los negocios de la Administración para el Año Fiscal anterior.

(b) Un informe completo sobre la situación y progreso de todos sus proyectos y actividades desde la creación de la Administración o desde la fecha de su último informe.

Sección 13.—Esta ley empezará a regir inmediatamente después de su aprobación.

Para enmendar el inciso (6) del Artículo 14 y el Artículo 17 de la Ley núm. 22 de 22 de abril de 1931, según enmendada, que crea el Tribunal Examinador de Médicos.

Decrétase por la Asamblea Legislativa de Puerto Rico:

Sección 1.—Se enmienda el inciso (6) del Artículo 14 de la Ley núm. 22 de 22 de abril de 1931, según enmendada, para que lea como sigue:

"Artículo 14.—

Toda persona que aspire a obtener licencia para ejercer en el Estado Libre Asociado de Puerto Rico la profesión de médico cirujano o la de osteópata, deberá cumplir con los siguientes requisitos:

(1) .....

(2) .....

(6) Practicar por un período mínimo de un año y máximo de dos años como médico donde el Consejo General de Salud determine que sus servicios profesionales sean de mejor utilidad en el sector público mediante autorización especial expedida al efecto por el Tribunal Examinador de Médicos y bajo la supervisión de dicho Tribunal. Esta autorización deberá indicar el pueblo o pueblos donde el aspirante habrá de practicar esos dos años, la fecha de su expedición y las fechas de comienzo y expiración de la autorización. Tal autorización podrá expedirse sólo después que el aspirante haya aprobado los exámenes a que se refiere el Artículo 11 de esta ley. Este requisito es adicional al requisito de internado y a cualquier período de residencia que el aspirante complete.

El período de servicio requerido por este inciso podrá cumplirse concurrentemente con los compromisos de prestación de servicios contraídos o que se contraigan en el futuro con el Estado Libre Asociado por razón de la ayuda económica que se reciba durante el período de estudios."

Sección 2.—Se enmienda el Artículo 17 de la Ley núm. 22 de 22 de abril de 1931, según enmendada, para que lea como sigue:

"Artículo 17.—

El Tribunal expedirá una licencia provisional especial autorizando la práctica de la medicina y cirugía en Puerto Rico, a todo médico cirujano que muestre evidencia de haber sido aceptado a un programa de internado y residencia en un hospital aprobado por el Tribunal, que haya aprobado aquella parte del examen de reválida que el Tribunal tenga a bien exigir, y que cumpla con todos los demás requisitos que exija la ley, disponiéndose que en el caso de médicos cirujanos extranjeros que estén tramitando su residencia permanente en Puerto Rico, deberán además de lo anterior, someter evidencia de los trámites llevados a cabo ante el Departamento de Inmigración y una declaración jurada de su intención de residir en Puerto Rico con carácter de permanencia.

Dicha licencia provisional especial será expedida por el término de un año y podrá renovarse por un año adicional, disponiéndose que este término podrá extenderse por un tercer año en aquellos casos especiales en que el Tribunal así lo considere necesario.

En el caso de ciudadanos extranjeros que deseen hacer su entrenamiento post graduado en Puerto Rico, el Tribunal tendrá discreción para por reglamento exigir los requisitos que crea conveniente mediante reglamento y extender la licencia provisional especial mientras completa dicho entrenamiento.

No obstante lo dispuesto anteriormente, todo aspirante a una licencia para ejercer en el Estado Libre Asociado de Puerto Rico la profesión de médico cirujano o la de osteópata, deberá cumplir con todos los requisitos dispuestos en el Artículo 14 de esta ley que le sean aplicables.

La omisión de este requisito constituirá práctica ilegal de la medicina en Puerto Rico y estará sujeta a la penalidad dispuesta en el Artículo 9 de esta ley."

Sección 3.—Esta ley comenzará a regir inmediatamente después de su aprobación.

Para adicionar el Capítulo 41 a la Ley núm. 77 de 19 de junio de 1957, según enmendada, conocida como "Código de Seguros de Puerto Rico".

Decrétase por la Asamblea Legislativa de Puerto Rico:

Sección 1.—Se adiciona un Capítulo 41 a la Ley núm. 77 de 19 de junio de 1957, según enmendada, conocida como Código de Seguros de Puerto Rico, para que lea como sigue:

CAPITULO 41

Artículo 41.010.—Definiciones

Para efectos de este capítulo, los siguientes términos tendrán el significado que a continuación se expresa:

(1) Profesional en el Cuidado de Salud—Significa cualquier persona, debidamente autorizada bajo las leyes del Estado Libre Asociado de Puerto Rico que actuando como principal ejerza las profesiones de médico cirujano, osteópata y odontología.

(2) Institución para el Cuidado de Salud—Significa cualquier facilidad u organización dedicada al cuidado y mantenimiento de la salud de un paciente, autorizada a tenor con las leyes del Estado Libre Asociado de Puerto Rico, excepto las del Estado Libre Asociado de Puerto Rico, sus dependencias, instrumentalidades y municipios y los asilos de fines no pecuniarios según se define este término en la Ley núm. 101 del 26 de junio de 1965, según enmendada.

(3) Paciente—Significa cualquier persona que por contrato explícito o implícito reciba o debía haber recibido cuidado o servicio de salud de un profesional en el cuidado de salud o de una institución para el cuidado de salud.

(4) Daño por Culpa o Negligencia (Malpractice)—Significa cualquier daño ocasionado a un paciente por error, omisión, culpa o negligencia como consecuencia de o inherentes a servicios profesionales brindados o que debieron haber sido brindados por un profesional en el cuidado de salud o una institución para el cuidado de salud.

(5) Cuidado o Servicio de Salud—Significa cualquier acto, acción o tratamiento prestado, o que debió haber sido prestado por un profesional en el cuidado de salud o una institución para el cuidado de salud a un paciente.

(6) Seguro de Responsabilidad Profesional Médico-Hospitalaria—Significa la cubierta de seguro de responsabilidad profesional para profesionales en el cuidado de salud e instituciones para el cuidado de salud que se establece bajo este capítulo.

(7) Solicitante Cualificado—Significa cualquier profesional en el cuidado de salud o institución para el cuidado de salud que solicite y no haya podido obtener seguro de responsabilidad profesional médico-hospitalaria en el mercado normal. Se entiende por mercado normal aquel compuesto por los aseguradores autorizados a suscribir seguro de responsabilidad profesional médico-hospitalaria.

(8) Asociación—Significa la Asociación de Suscripción Conjunta de Seguro de Responsabilidad Profesional Médico-Hospitalaria.

(9) Administración—Significa la Administración del Fondo de Compensación al Paciente.

(10) Plan—Significa el Plan de Operaciones de la Asociación.

(11) Secretario—Significa el Secretario de Hacienda.

(12) Junta—Significa la Junta de Directores de la Administración.

(13) Director—Significa el Director Ejecutivo de la Administración.

Artículo 41.020.—Programa de Seguro de Responsabilidad Profesional Médico-Hospitalaria

Por la presente se establece un programa de seguro de responsabilidad profesional médico-hospitalaria en el Estado Libre Asociado de Puerto Rico, el cual será instrumentado conforme a las disposiciones de este capítulo.

Este programa y sus actividades se llevarán a cabo conforme se dispone más adelante, a través de aseguradores autorizados a contratar seguros en Puerto Rico, una Asociación de Suscripción Conjunta de Aseguradores y una Administración del Fondo de Compensación al Paciente ambas creadas por este capítulo.

Artículo 41.030.—Participación de Aseguradores

Todo asegurador autorizado para contratar seguro de accidente podrá participar en la emisión de las pólizas que contempla este programa para cubrir la responsabilidad financiera que más adelante se le requiere a los profesionales en el cuidado de salud y a las instituciones para el cuidado de salud de acuerdo con este capítulo.

Artículo 41.040.—Asociación de Suscripción Conjunta y Plan de Operaciones

(1) Por la presente se crea una Asociación de Suscripción Conjunta de Seguro de Responsabilidad Profesional Médico-Hospitalaria para proveer dicho seguro a solicitantes cualificados. La Asociación estará compuesta por todos los aseguradores autorizados en Puerto Rico para contratar seguro contra accidente, según se define en los apartados (1) y (10) del Artículo 4.080. Dichos aseguradores deberán ser miembros de la Asociación y su participación en tal Asociación será condición indispensable para poder continuar suscribiendo seguros en el Estado Libre Asociado de Puerto Rico.

(2) El propósito de la Asociación es proveerle seguro de responsabilidad profesional médico-hospitalaria por los límites de responsabilidad financiera establecidos en el Artículo 41.080 a los solicitantes cualificados y promover al máximo la competencia entre aseguradores financieramente sólidos.

(3) La Asociación tendrá, con respecto al seguro de responsabilidad profesional médico-hospitalaria, poder para expedir pólizas de seguro a solicitantes cualificados, asumir reaseguro de sus miembros y ceder reaseguro. La Asociación podrá delegar en uno o más de sus miembros, que así lo deseen, o en cualquier otra entidad

para que provea servicios a sus pólizas y reclamaciones a nombre de la Asociación.

(4) La Asociación operará bajo la supervisión y dirección de una Junta de Directores que consistirá de nueve de los aseguradores que participen en la Asociación quienes serán electos por los miembros de ésta. La Junta de Directores de la Asociación se elegirá anualmente en una reunión de los miembros o sus representantes autorizados en la fecha y lugar que designe el Comisionado. Los votos de los miembros en tal elección tendrán peso en la proporción que las primas netas directas suscritas por cada miembro durante el año anterior guarde con las primas netas directas suscritas en Puerto Rico por todos los miembros de la Asociación en dicho año para el seguro contra accidentes descrito en el apartado (1) de este artículo. El Presidente será electo de entre los miembros de la Junta de Directores de la Asociación.

(5) La Asociación deberá funcionar por un período que no excederá de ocho años desde la fecha de vigencia de esta ley, y podrá ser disuelta por el Comisionado, previa celebración de vistas públicas, en cualquier momento antes si determina que no es necesaria y que existe o que se ha mantenido un mercado adecuado para dicho seguro por la industria de seguros. El Comisionado podrá prorrogar la existencia de la Asociación por un período que no excederá de cuatro años adicionales.

(6) La Asociación proveerá seguro de responsabilidad profesional médico-hospitalaria en un formulario de póliza uniforme para todos los profesionales en el cuidado de salud e instituciones para el cuidado de salud. Dicho formulario de póliza uniforme cumplirá con los requisitos exigidos en el Capítulo 11 del Código de Seguros.

(7) La Asociación tendrá poder para demandar y ser demandada y negociar aquellos contratos que sean propios para llevar a cabo sus propósitos.

(8) La Asociación deberá adoptar, dentro de sesenta (60) días después de su establecimiento, un plan de operaciones. Dicho plan estará sujeto a la aprobación del Comisionado y entrará en vigor diez (10) días después de haber sido aprobado por él. Si el Comisionado desaprueba el plan, en todo o en parte, los directores de la Asociación, dentro de los quince (15) días laborables

siguientes a la notificación de dicha desaprobación someterán el plan, o la parte objetada enmendada y revisada y de no someter dicha nueva propuesta o de no resultar ésta aceptable, el Comisionado promulgará su propio plan, o la correspondiente parte del mismo, según sea el caso.

El plan proveerá para una administración económica, justa y no discriminatoria y para un pronto y eficiente mercadeo del seguro de responsabilidad profesional médico-hospitalaria, que en beneficio del bienestar general y la seguridad de los solicitantes cualificados permita una equitativa distribución de los riesgos asegurables. Este plan deberá contener disposiciones sobre, pero sin limitarse a:

(a) La administración de la Asociación y la elección del Presidente y cualesquiera otros oficiales que la Junta de Directores estime necesarias.

(b) (i) Tipos, planes de tarifas y reglas de tarifaje aplicables al seguro suscrito por la Asociación y las estadísticas relacionadas con el mismo pero sujeto todo esto a las disposiciones del capítulo 12 de este Código.

(ii) Las reglas y planes de tarifaje inscritas en cuanto al Plan podrán proveer normas para la aplicación de recargos para riesgos con experiencia adversa. Tales reglas y planes de tarifaje proveerán para la pronta eliminación de dichos recargos cuando la experiencia se normalice.

(iii) Las reglas y planes de tarifaje podrán proveer normas para la clasificación de riesgos que reflejen la experiencia de pérdidas y gastos en las diferentes especialidades de práctica de los profesionales en el cuidado de salud o instituciones para el cuidado de salud.

(c) Reglas para instrumentar la disolución del plan a su terminación.

(9) El Comisionado de Seguros, antes de la terminación de la Asociación determinará si existe una necesidad razonable para continuar ofreciendo cubierta a aquellos que hayan sido asegurados por la Asociación en cuanto a reclamaciones únicamente por daños que ocurrieran durante la existencia de ésta. Si se encontrara tal necesidad, el Comisionado de Seguros deberá establecer un plan para la adquisición de tal cubierta tomando en consideración los términos de prescripción establecidos en el Artículo 41.090.

(10) Todos los aseguradores miembros de esta Asociación participarán en sus ganancias y pérdidas en la proporción que las primas netas directas de cada miembro (excluyendo la porción de primas que corresponda a las operaciones de la Asociación) suscritas durante el año anterior guarde con las primas netas directas totales suscritas en Puerto Rico por todos los miembros de la Asociación en dicho año para el seguro de accidente.

Artículo 41.050.—Administración del Fondo de Compensación al Paciente; Límites de Responsabilidad

(1) (a) Se crea la Administración del Fondo de Compensación al Paciente cuyo propósito será proveer una cubierta básica de responsabilidad profesional médico-hospitalaria hasta la suma de $500,000 para cubrir aquella porción de cada reclamación de daños por culpa o negligencia (malpractice) que ocurra en Puerto Rico y que exceda los límites de responsabilidad financiera que se requiere en el Artículo 41.080 a los profesionales en el cuidado de salud y a las instituciones para el cuidado de salud. En ningún caso la Administración será responsable por una cantidad en exceso de quinientos mil (500,000) dólares por ocurrencia y quinientos mil (500,000) dólares agregados, excepto cuando el asegurado hubiera obtenido y pagado una cubierta según se dispone en el apartado (c), en cuyo caso el límite de tal cubierta será el máximo. Disponiéndose, que esta agencia estará comprendida dentro del término administradores individuales según se provee en la Ley núm. 5 del 14 de octubre de 1975.

(b) A la Administración ingresará la aportación que se le impone a los profesionales en el cuidado de salud y a las instituciones para el cuidado de salud conforme se dispone en el Artículo 41.060. La Administración será también responsable por el pago de gastos razonables y necesarios incurridos en el pago de reclamaciones y por sus gastos administrativos.

(c) La Administración podrá proveer una cubierta opcional a los profesionales en el cuidado de salud e instituciones para el cuidado de salud en exceso de quinientos mil (500,000) dólares pero no mayor de un millón (1,000,000) de dólares siempre y cuando que el profesional en el cuidado de salud o la institución para el cuidado de salud haga la aportación correspondiente.

(2) La Administración operará bajo la supervisión y dirección de una Junta de Directores que consistirá del Comisionado de Seguros, quien será su Presidente, del Secretario de Salud, y los presidentes de los tribunales o juntas examinadoras de los profesionales en el cuidado de salud cubiertos por este capítulo. La Junta designará y fijará el sueldo de un Director Ejecutivo a quien delegará la operación directa de la Administración. La Junta tendrá las siguientes facultades y obligaciones:

(a) Por lo menos trimestralmente cada año, celebrar reuniones ordinarias y aquellas sesiones extraordinarias que se estimen necesarias. La Junta llevará actas completas de todos sus procedimientos.

(b) Considerar y aprobar el presupuesto anual de la Administración y cualesquiera otros acuerdos que le refiera el Director Ejecutivo.

(c) Tan pronto como sea posible después de finalizar cada año económico pero a más tardar el primero de noviembre de cada año, revisar, aprobar y ordenar que se transmita al Gobernador y a la Asamblea Legislativa un informe anual que contenga entre otras cosas, un balance de situación económica; un estado de ingresos y desembolsos para el año; estados detallados acerca de la experiencia de reclamaciones de la Administración para el año, un informe sobre los títulos de inversión propiedad de la Administración; una evaluación que incluya entre otras cosas lo siguiente: el impacto del programa en la solución del problema de malpractice; el ámbito y la extensión del problema de responsabilidad profesional médico-hospitalaria en ese momento; nuevas alternativas y soluciones al problema; disponibilidad del seguro para otras profesiones; y otros datos estadísticos y financieros que se consideren necesarios para una adecuada interpretación de la situación de la Administración y del resultado de sus operaciones.

(d) Fijar las aportaciones que se establecen en el Artículo 41.060.

(e) Investigar y resolver extrajudicialmente con la aprobación del demandado, cualquier reclamación contra la Administración.

(f) Cualquier otro poder o facultad necesaria para llevar a cabo los propósitos de este capítulo.

(g) Aprobar reglas y reglamentos promulgados por el Administrador.

(3) (a) La Administración tendrá facultad para demandar y ser demandada por cualquier reclamación que surja contra, o en relación con la misma, de acuerdo con lo dispuesto en este capítulo, y tendrá cualquier otro poder y facultad necesaria para instrumentar los propósitos de este capítulo.

(b) Se faculta a la Administración a organizar las unidades administrativas y contratar los servicios o estudios que sean necesarios para instrumentar las funciones de la misma.

(c) Se le faculta, además, para contratar los servicios de abogados, técnicos y especialistas que crea necesarios a fin de proteger los intereses de la Administración en toda acción en que ésta se incluya como parte de una demanda.

(d) Previa aprobación de la Junta, promulgar reglas y reglamentos para el funcionamiento de la Administración.

(4) Los gastos de la Administración se sufragarán de acuerdo al presupuesto aprobado por la Junta y se harán con cargo a la cuenta especial que se indica en el inciso (5) que sigue.

(5) Las aportaciones a la Administración se pagarán al Secretario por conducto del Director. El Secretario depositará en una cuenta especial para la Administración dichas aportaciones y sólo efectuará desembolsos debidamente cumplimentados mediante comprobantes de desembolsos autorizados por el Director.

(6) Anualmente, el Secretario preparará un informe del estado del Fondo y le remitirá copia a la Administración. El informe deberá incluir ingresos, egresos y toda otra información pertinente para la determinación de cualquier tipo de aportación al Fondo. Mensualmente someterá a la Administración un informe de ingresos, egresos y balance de su cuenta especial.

(7) Al cierre de operaciones de cada año económico el dinero retenido en la cuenta especial deberá ser invertido por el Secretario en inversiones garantizadas que produzcan intereses a corto plazo. Todo ingreso derivado de tales inversiones deberá acreditarse a la cuenta especial de la Administración. Los dineros retenidos en dicha cuenta no podrán ser utilizados para propósitos distintos a los contemplados por este capítulo.

(8) Ningún acreedor por sentencia o cualesquiera otros reclamantes podrá embargar la totalidad o parte de las cuentas de la Administración dispuesto por este capítulo.

Artículo 41.060.—Fijación y Pago de Aportaciones al Fondo

(1) Anualmente, cada profesional en el cuidado de salud e institución para el cuidado de salud que preste activamente servicios en Puerto Rico vendrá obligado a pagar a la Administración la aportación establecida por ésta para la cubierta básica provista en el Artículo 41.050(1)(a).

La aportación del primer año será de cien (100) dólares para aquellos profesionales en el cuidado de salud, médicos, osteópatas y odontólogos generalistas que no lleven a cabo cirugía, de quinientos (500) dólares para los demás profesionales en el cuidado de salud; y de cincuenta (50) dólares por cama para las instituciones para el cuidado de salud o aquella cantidad que la Junta considere adecuada de acuerdo a la naturaleza del riesgo de dichas instituciones. En caso de que los asegurados antes indicados deseen la cubierta opcional que se menciona en el Artículo 41.050(1)(d) aportarán al Fondo adicionalmente $50, $200 y $15, respectivamente. El primer año comenzará el 1 de julio de 1976 y seguirá adelante en base a un año fiscal.

(2) Después del primer año de operaciones, la Junta, luego de consultar con la Oficina del Comisionado de Seguros determinará e impondrá aportaciones basadas en las siguientes consideraciones:

(a) Experiencia pasada y prospectiva de pérdidas y gastos en los diferentes tipos de práctica y en las diferentes áreas de responsabilidad.

(b) Experiencia anterior de reclamaciones contra personas u hospitales cubiertos bajo este capítulo.

(c) Factores de riesgos para personas retiradas, semi-retiradas o profesionales a tiempo parcial.

(d) La cantidad y solvencia de la Administración en un año dado.

Para fijar las aportaciones la Junta podrá consultar con un organismo tarifador.

(3) En la determinación de la aportación para la cubierta opcional provista en el Artículo 41.050(1)(c) la Junta utilizará los criterios establecidos en este artículo.

(4) Si la cantidad de dinero aportada a la Administración no es suficiente para satisfacer las reclamaciones hechas contra ésta en un año específico, la Junta requerirá una aportación proporcional adicional a todos los participantes para ese año fiscal. La Junta deberá imponer tal aportación adicional a los participantes en cantidades que razonablemente reflejen la exposición al riesgo dentro de las clasificaciones que hubiera prescrito y hasta el monto que sean suficientes para obtener el dinero necesario para responder por todas las reclamaciones de dicho año fiscal.

(5) Dicha aportación deberá pagarse antes del 1 de julio de cada año fiscal. Si la misma no se paga en la fecha provista, la Administración notificará a los Tribunales o Juntas Examinadoras de Profesionales en el cuidado de salud y/o al Secretario de Salud para que tomen la acción dispuesta específicamente para estos casos.

Artículo 41.070.—Reclamaciones Contra la Administración

(1) Cualquier persona que radique una demanda contra un profesional en el cuidado de salud o institución para el cuidado de salud no podrá recobrar porción alguna de la Administración, a menos que se le emplace o sea incluido como parte en el pleito.

(2) Cuando a juicio del Administrador la disponibilidad de fondos para el pago total de las reclamaciones en su poder no fuere suficiente, tendrá facultad para determinar la forma y manera en que habrá de hacer efectivo el pago de la adjudicación en exceso de cien mil (100,000) dólares que se proveen en este capítulo. Disponiéndose que en ningún caso la Administración responderá por daños por culpa o negligencia (malpractice) ocasionados en un año fiscal para el cual el profesional en el cuidado de salud o institución para el cuidado de salud no haya cumplido con las aportaciones exigidas en el Artículo 41.060. Para cualquier transacción extrajudicial que exceda cien mil (100,000) dólares, que pudiera requerir un pago de la Administración se requerirá la aprobación de ésta.

(3) Será obligación del asegurador que emita una cubierta de responsabilidad profesional médico-hospitalaria a un profesional en el cuidado de salud o institución para el cuidado de salud cubierto por la Administración, incurrir en aquellos gastos que sean necesarios para proveer una defensa adecuada para cualquier reclamación radicada.

(4) Las reclamaciones extrajudiciales radicadas contra la Administración serán pagadas en el orden en que hayan sido recibidas dentro de noventa (90) días después de radicadas, a menos que sean rechazadas por la Administración. En caso de una sentencia ésta se pagará dentro del término de 90 días a partir de la fecha en que se convierta en final y firme. Si la Administración no tiene suficiente dinero en su cuenta especial en un año fiscal para pagar todas las reclamaciones, aquellas recibidas después de agotada dicha cuenta deberán pagarse inmediatamente en el año fiscal siguiente en el orden en que fueron recibidas.

(5) La Administración no quedará sujeta al pago de intereses sobre sentencias que le afecten.

(6) Si un profesional en el cuidado de salud o institución para el cuidado de salud tiene cubierta en exceso de $100,000, ésta será responsable por pérdidas hasta la cantidad de la misma, y éste deberá recibir una reducción actuarial adecuada a su aportación a la Administración. Tal reducción deberá concederse únicamente después que la persona haya demostrado a satisfacción de la Administración que tiene tal cubierta.

Artículo 41.080.—Responsabilidad Financiera

(1) Todo profesional en el cuidado de salud y/o institución para el cuidado de salud deberá radicar ante la Administración prueba de su responsabilidad financiera por la cantidad de cien mil (100,000) dólares, por ocurrencia o hasta un agregado de trescientos mil (300,000) dólares por año, excepto aquellos profesionales en el cuidado de salud que exclusivamente prestan sus servicios para el Estado Libre Asociado de Puerto Rico, sus dependencias, instrumentalidades y municipios y aquellas instituciones para el cuidado de salud que pertenezcan al Estado Libre Asociado de Puerto Rico, sus dependencias, instrumentalidades y municipios. Dicha prueba de responsabilidad financiera deberá ser remitida a la Administración antes del 1 de julio de cada año y cubrirá su responsabilidad durante el año fiscal siguiente.

Ningún profesional en el cuidado de salud que trabaje exclusivamente para el Estado Libre Asociado de Puerto Rico, sus dependencias, instrumentalidades y municipios podrá ser incluido como parte demandada en una demanda de daños por culpa o negligencia que cause en el desempeño de su profesión mientras actúe en cumplimiento de sus deberes y funciones como empleado del Estado Libre Asociado de Puerto Rico, sus dependencias, instrumentalidades y municipios.

(2) Todo profesional en el cuidado de salud y/o institución para el cuidado de salud deberá demostrar su responsabilidad financiera para el año fiscal en que ejercerá sus funciones en una de las siguientes maneras:

(a) Establecer una cuenta de plica ("escrow fund") por la cantidad de trescientos mil (300,000) dólares no girables sin la autorización de la Administración.

(b) Haber obtenido un seguro de responsabilidad profesional médico-hospitalaria por la cantidad de cien mil (100,000) dólares por ocurrencia o hasta un agregado de trescientos mil (300,000) dólares por año, de aseguradores privados o de la Asociación si estuviere en funciones. Dicho contrato de seguro contendrá una disposición a los efectos de que el asegurador notificará previamente a la Administración la cancelación del seguro.

(3) Si un profesional en el cuidado de salud y/o institución para el cuidado de salud no cumple con las disposiciones sobre responsabilidad financiera establecida en este artículo, la Administración notificará a los Tribunales o Juntas Examinadoras de Profesionales en el cuidado de salud y/o al Secretario de Salud para que tomen la acción dispuesta específicamente para estos casos.

Artículo 41.090.—Términos de Prescripción

(1) Los términos de prescripción contenidos en este artículo serán los únicos aplicables a las acciones de daños por culpa o negligencia (malpractice) que se inicien contra profesionales en el cuidado de salud e instituciones para el cuidado de salud.

La acción por alegados daños por culpa o negligencia (malpractice) comenzará, independientemente de lo dispuesto en otra ley, dentro de un año a partir de la fecha en que ocurrió el daño que dio lugar a la acción, o dentro de un año desde el momento en que el daño fue descubierto o debió haber sido descubierto con la debida diligencia. En ningún caso se podrá iniciar la acción más tarde de dos años desde la fecha en que ocurrió el daño que dio lugar a la causa de acción.

(2) En aquellas acciones cubiertas por este artículo en que se demuestre que por fraude, ocultación o falsa representación de hechos se impidió el descubrimiento del daño dentro del período de dos años, el término de prescripción se extenderá indefinidamente.

(3) Con respecto a los menores e incapaces los términos de prescripción serán aquellos establecidos en los apartados (1) y (2) de este artículo y comenzarán a partir de la fecha en que alcancen la mayoría de edad o cese la incapacidad.

(4) Las acciones de daños por culpa o negligencia (malpractice) contra profesionales en el cuidado de salud e instituciones para el cuidado de salud ocurridos antes de la fecha de vigencia de esta ley se regirán por los términos prescriptivos dispuestos por leyes vigentes al ocurrir el daño.

Artículo 41.100.—Arbitraje de Reclamaciones por Culpa o Negligencia

Toda acción civil que surja de una reclamación de daños por culpa o negligencia (malpractice) se iniciará mediante la radicación de una demanda en la sala del Tribunal Superior competente. El tribunal procederá a someter la reclamación a arbitraje según se dispone en el Artículo 41.110. En aquellos casos en que alguna de las partes no cuente con medios suficientes para pagar los costos del panel de arbitraje deberá hacerlo constar mediante alegación en la demanda.

Artículo 41.110.—Inicio del Procedimiento y Designación del Panel de Arbitraje

(1) Una vez transcurridos sesenta (60) días de radicada la contestación a la demanda en una reclamación de daños por culpa o negligencia (malpractice), o en cualquier momento antes, que las partes notificaren estar preparadas, el Juez Administrador de la sala del Tribunal Superior competente designará dentro de los próximos treinta (30) días un panel de arbitraje que entenderá en el arbitraje de la reclamación y la sala o el lugar donde se reunirá dicho panel.

(2) El panel de arbitraje tendrá funciones cuasi-judiciales y estará compuesto por tres miembros, un abogado que será su Presidente, un miembro de la profesión médica, que pertenecerá a la clase a la cual pertenezca la persona contra quien se haya radicado la acción y un representante del interés público que no será abogado ni profesional en el cuidado de salud ni representante de institución para el cuidado de salud.

(3) Los miembros del panel de arbitraje se seleccionarán de un listado de candidatos a ser preparado por el Secretario de Salud dentro de los treinta (30) días después de la aprobación de esta ley. En años sucesivos el Secretario de Salud preparará dicho listado dentro de los noventa (90) días después de la terminación del año natural, disponiéndose que mientras no se sometan los nuevos listados permanecerán en uso los listados anteriores. En la preparación de este listado el Secretario de Salud podrá aceptar las recomendaciones hechas por las asociaciones médicas reconocidas y por el Colegio de Abogados de Puerto Rico en cuanto a los candidatos que en su campo a cada una de esas organizaciones corresponda recomendar.

En la preparación de dicho listado, el Secretario de Salud podrá agrupar los candidatos tomando en consideración su especialidad y residencia dentro de la demarcación territorial de la competencia de la sala del Tribunal Superior correspondiente. Lo anterior no constituye una limitación para que en el panel de arbitraje se designen miembros de áreas distintas a la sala del Tribunal correspondiente.

(4) (a) El Juez Administrador discrecionalmente fijará una dieta a cada panelista que no excederá de $100 diarios por panelista; disponiéndose que cualquiera de los panelistas podrá renunciar a su dieta. El importe total de la dieta al igual que los gastos en que incurra el panel de arbitraje al conducir las vistas, será sufragado proporcional al número de partes en la demanda, excepto que el tribunal tendrá discreción para relevar a cualquiera de las partes total o parcialmente del pago proporcional de la dieta si se demuestra que los recursos económicos de dicha parte no le permitirán efectuar el pago, en cuyo caso la parte aportará la cantidad que determine el tribunal y el remanente será sufragado a prorrata entre las demás partes de la demanda.

(b) El importe de la dieta y los gastos en que incurra el panel de arbitraje se consignarán en el tribunal dentro de quince (15) días a partir de la fecha de terminación de los procedimientos establecidos en el Artículo 41.130(1). El Secretario del tribunal los remitirá a los panelistas dentro de los treinta (30) días siguientes de emitida la decisión del panel de arbitraje.

(5) La no comparecencia de cualquiera de las partes, sus testigos, o abogados que ocasionen la suspensión de cualquier vista debidamente notificada, salvo en caso de aviso previo de no comparecer por causa justificada y este aviso dado con no menos de tres (3) días de antelación a la fecha fijada para la vista conllevará el pago, por la parte que ocasione la suspensión, de la dieta fijada para los miembros del panel.

(6) Cualquiera de las partes podrá objetar la designación de un miembro del panel de arbitraje luego de mostrar causa justificada para ello pudiendo el tribunal sustituirlo a su discreción.

Artículo 41.120.—Juramentación de los Miembros del Panel de Arbitraje; Procedimientos

(1) Antes de la vista los miembros del panel de arbitraje prestarán juramento ante un Magistrado haciendo constar que oirán la prueba presentada y emitirán una decisión justa y equitativa. Una vez juramentados quedan facultados para tomar juramento.

(2) El panel de arbitraje presidirá las vistas, fijará la hora de las mismas y notificará a las partes. Puede, además, suspender o posponer la vista y ejercerá todos los poderes necesarios para conducir las mismas. El tribunal donde se radicó la acción de daños por culpa o negligencia (malpractice), a petición de parte, puede ordenar al panel de arbitraje que proceda sin dilación con la vista.

(3) El panel de arbitraje llevará una minuta exacta y concisa de los procedimientos de la vista y un récord taquigráfico o en cintas magnetofónicas de la misma.

(4) El testimonio de los testigos será bajo juramento. Las partes tienen derecho a presentar evidencia y a contrainterrogar testigos. La parte demandante deberá presentar evidencia a los efectos de que con posterioridad a los hechos que dan lugar a la demanda ha consultado con otros facultativos sobre los mismos. Las Reglas de Procedimiento Civil para el Tribunal General de Justicia regirán los procedimientos ante el panel de arbitraje; las Reglas de Evidencia serán de aplicación en los procedimientos efectuados ante el panel.

(5) El panel de arbitraje puede celebrar la vista y emitir la decisión cuando una parte debidamente notificada no haya comparecido a la vista en tres ocasiones consecutivas.

(6) El panel de arbitraje podrá ordenar la comparecencia de testigos, la presentación de prueba documental y cualquier otra evidencia necesaria. Las citaciones se expedirán por el tribunal a petición de parte o del panel de arbitraje y se notificarán y harán cumplir en la misma forma como si se tratase de una acción civil.

(7) El panel de arbitraje, previa oportunidad de las partes de seleccionar un perito común, y de éstas no hacerlo, podrá solicitar del tribunal donde se radicó la acción de daños por culpa o negligencia (malpractice), que designe el perito o los peritos necesarios para que rindan los informes y presten testimonio sobre aquellas reclamaciones que se someten a arbitraje.

(8) Las vistas se celebrarán ante la presencia de todos los miembros del panel de arbitraje.

Artículo 41.130.—Decisión del Panel

(1) Los procedimientos ante el panel de arbitraje se llevarán a cabo dentro del término de noventa (90) días a partir de la fecha en que éste haya sido nombrado. Disponiéndose que el tribunal, a solicitud del panel de arbitraje y por causa justificada podrá prorrogar dicho término hasta un máximo que no excederá de noventa (90) días adicionales.

(2) El panel de arbitraje emitirá su decisión por mayoría dentro de sesenta (60) días después de terminados los procedimientos ante el mismo. Dicha decisión consistirá de sus determinaciones de hechos, conclusiones de derecho, recomendaciones sobre daños y responsabilidad y sus fundamentos.

(3) La decisión será firmada por todos los miembros del panel de arbitraje, pero cualquiera de sus miembros puede emitir por escrito una opinión disidente o concurrente exponiendo las razones para la misma.

(4) La decisión se radicará ante la sala del tribunal donde se radicó la acción de daños por culpa o negligencia (malpractice) y el tribunal expedirá la resolución correspondiente.

(5) Una vez dictada la resolución y ésta sea final y firme, la parte perdidosa vendrá obligada a resarcir a la otra parte por todos aquellos gastos en que ésta haya realmente incurrido y que no hayan sido cubiertos por las costas que le fueron adjudicadas en el procedimiento.

(6) La decisión del panel de arbitraje será final y solo podrá ser revocada o modificada por dicho tribunal si luego de revisada la misma encontrare que:

(a) las determinaciones de hechos incluidas en la decisión son claramente erróneas; o
(b) la decisión no fue emitida conforme a derecho; o
(c) no se llevaron a cabo los procedimientos necesarios para la emisión de la decisión.

(7) Los miembros del panel de arbitraje tendrán absoluta inmunidad respecto a sus expresiones y recomendaciones mientras actúen dentro del marco oficial en su capacidad como tal.

Artículo 41.140.—Procedimientos Posteriores a Decisión del Tribunal

(1) De la resolución del tribunal las partes podrán recurrir en revisión ante el Tribunal Supremo de Puerto Rico.

Artículo 41.150.—Informes

(1) Todos los aseguradores y/o la Asociación de Suscripción Conjunta deberá someter a la Oficina del Comisionado de Seguros, en la forma requerida por éste, informes mensuales de todas y cada una de las reclamaciones y/o resoluciones de los tribunales que por concepto de daños por culpa o negligencia (malpractice) les fueran hechas. Esta información deberá estar en la Oficina del Comisionado de Seguros en o antes del décimo día siguiente a la terminación del mes anterior. El incumplimiento de este requisito será sancionado por el Comisionado de Seguros de acuerdo a lo dispuesto en el Artículo 3.210 de este Código.

(2) A solicitud de la Administración el tribunal expedirá, libre de derechos, copia certificada de la resolución y de la decisión del panel de arbitraje.

(3) La Administración remitirá las resoluciones de los tribunales y/o las adjudicaciones extrajudiciales sobre daños por culpa o negligencia (malpractice) dentro de los treinta (30) días de haberlas recibido al Secretario de Salud y/o a los Tribunales o Juntas Examinadoras de profesionales en el cuidado de salud, según sea el caso, para que se tome la acción disciplinaria que corresponda contra el profesional en el cuidado de salud o institución para el cuidado de salud.

(1) Si cualquier disposición de esta ley o la aplicación de la misma a cualquier persona o circunstancia fuere declarada inconstitucional o nula, dicha nulidad no afectará las demás disposiciones ni la aplicación de esta ley que pueda tener efecto sin necesidad de las disposiciones o aplicaciones que hubieran sido declaradas nulas, y a tal fin se declara que las disposiciones de esta ley son separables unas de otras.

(2) Se asigna a la Administración, de fondos no comprometidos del Tesoro Estatal, la suma de doscientos cincuenta mil (250,000) dólares, como capital inicial para gastos de administración. La suma así asignada será en calidad de anticipo y deberá ser devuelta al fondo general tan pronto como la situación financiera de la Administración así lo permita. La Junta determinará la forma y tiempo de pago de dicha devolución.

(3) Las disposiciones de esta ley no aplicarán a reclamaciones por daños ocurridos con anterioridad a la fecha de efectividad de la misma.

Sección 2.—Esta ley comenzará a regir el 1 de julio de 1976.

Para regular el ejercicio de la Profesión de Optico y Técnicos de Laboratorio de Optica, para crear la Junta Examinadora de Opticos, definir sus poderes y fijar penalidades por infracciones a la ley.

Decrétase por la Asamblea Legislativa de Puerto Rico:

Artículo 1.—Definiciones: Para los efectos de esta ley los siguientes términos tendrán el significado que a continuación se indican:

a) Optico: Persona que se dedica a la preparación de cristales con foco, espejuelos, anteojos o sus accesorios, mediante recetas escritas expedidas por oftalmólogos u optómetras debidamente autorizados a ejercer su profesión y, considerando tales recetas escritas mide los contornos faciales del paciente o cliente y talle, pule y corte y monte cristales oftálmicos, que lleve la receta de médico oftalmólogo u optómetra para determinar el tamaño y forma de montura y lentes que mejor se ajuste a las necesidades físicas de dicha persona. También hace duplicados, reparaciones y repeticiones de los lentes sin necesidad de una nueva receta.

b) Técnicos de Laboratorios de Optica: Persona que se dedica a tallar, pulir, cortar y montar lentes oftálmicos; pero que no está capacitado para abrir una tienda de óptica donde se atienda a personas que llevan recetas de médico oftalmólogo u optómetra.

c) Junta Examinadora de Opticos de Puerto Rico.

d) Secretario Ejecutivo: Se referirá al Secretario Ejecutivo de la división de Juntas Examinadoras.

e) Práctica de la Optica: Se entenderá que está interviniendo en la práctica de la óptica toda aquella persona natural o jurídica que anuncie como que hace espejuelos, duplicados de cristales o de espejuelos, mide los contornos faciales del paciente o cliente que lleve la receta de médicos oftalmólogos u optómetras, para determinar el tamaño y forma de montura y lentes que mejor se ajuste a las necesidades de dicho paciente o cliente, y talle, pula, corte y monte cristales oftálmicos, y que abriere o tuviere una tienda, óptica, establecimiento, despacho o taller con ese objeto; disponiéndose, sin embargo, que toda tienda, óptica, establecimiento u oficina y que cumpla con las disposiciones y reglamentos de esta ley, podrá anunciar y vender al público espejuelos de lentes oftálmicos y/o cristales con o sin foco.

Nada de lo dispuesto en esta ley podrá interpretarse como:

1) Facultando al óptico a presentarse u ofrecerse para tratar por cualquier medio o método a examinar los ojos a diagnosticar, tratar, corregir, curar, operar o prescribir para ningún tipo de enfermedad o deficiencia o condición física en la vista.

2) Limitando o restringiendo el ejercicio de la medicina o la optometría. Disponiéndose, sin embargo, que ningún médico, oftalmólogo, u oculista se podrá dedicar a la práctica de la óptica o venta de espejuelos directa o indirectamente, ni podrá recomendar al paciente una óptica específica para la preparación de su receta cuando vaya a obtener un beneficio económico por dicha recomendación a no ser que tenga trabajando en su oficina un óptico graduado y debidamente autorizado por la Junta Examinadora de Opticos de Puerto Rico.

Artículo 2.—Por la presente se crea una Junta Examinadora de Opticos que constará de cinco miembros nombrados por el Gobernador, previa recomendación de la Junta Examinadora de Optómetras y que estará compuesta por tres ópticos y dos optómetras. Dichos tres ópticos deberán ser ciudadanos de los Estados Unidos, haber residido en Puerto Rico no menos de tres años inmediatamente antes de ser nombrados, tener diplomas de ópticos expedidos por colegios, universidades o escuelas reconocidas, y haber practicado la óptica en Puerto Rico por no menos de seis años. Desempeñarán sus cargos por un término de tres años o hasta que sus sucesores sean nombrados y tomen posesión, excepto que los primeros miembros de la Junta que se nombren desempeñarán sus cargos, uno por año, dos por dos años y dos por tres años en el orden en que los designe el Gobernador. Las vacantes que ocurran se cubrirán por el período que falta por expirar el término del miembro que ocasione la vacante. El Gobernador podrá destituir de la Junta a cualquier miembro de la misma por abandono de sus deberes, por práctica incorrecta en su profesión o por conducta inmoral luego de ser oído ante la Junta Examinadora de Opticos.

La Junta Examinadora de Opticos aprobará un Reglamento estableciendo los procedimientos internos de la Junta, la cual celebrará por lo menos cuatro sesiones ordinarias al año para resolver sus asuntos oficiales y llevar a cabo exámenes. Tres miembros de la Junta constituirán quórum.

Los miembros de la Junta recibirán $15.00 por cada día o porción del mismo que dediquen a sus deberes oficiales y tendrán derecho al cobro de diez (10) centavos por cada milla corrida para asistir a las reuniones. Estos pagos serán hechos de cualesquiera fondos no comprometidos del erario público.

Artículo 3.—Facultades y Deberes de la Junta.

a) La Junta Examinadora de Opticos deberá autorizar la práctica de los ópticos en Puerto Rico, quedando facultada para expedir las correspondientes licencias a todas las personas que reúnan los requisitos especificados en esta ley, y a aquellos miembros de la Junta que al entrar en vigor esta ley no tenga su licencia de óptica en Puerto Rico y que reúna los otros requisitos de ley, podrá darla al optómetra o el que el Gobernador nombre para la Junta.
b) La Junta llevará un libro de actas de todos sus procedimientos y organizará sus archivos de modo que queden registradas todas las solicitudes de ópticos hechas y anotará en libros adecuados sus resoluciones y actuaciones.

c) La Junta tendrá un registro que contendrá una lista de las licencias de ópticos que otorgue con los números correspondientes.

d) Dictará reglas y reglamentos para la administración interna de la Junta, sobre la admisión y práctica de la óptica, sobre la celebración de exámenes para admisión a la profesión de óptico y para establecer los procedimientos administrativos para las vistas de suspensión o cancelación de licencias de ópticos. Dichas reglas y reglamentos serán adoptados luego de celebrarse vistas públicas y entrarán en vigor después de ser publicadas en dos diarios de circulación general y radicadas en el Departamento de Estado.

Artículo 4.—Requisitos para obtener licencia.

a) Los solicitantes a licencia de ópticos mediante examen deberán llenar los siguientes requisitos mínimos:

1. Ser ciudadano de Estados Unidos de América, mayor de edad, y tener diploma de escuela superior o su equivalente, haber observado buena conducta y tener buena salud.

2. Diploma de óptico obtenido en escuela, colegio reconocido por la Junta, o de una escuela que cuando se otorgó el diploma estuviese reconocida por la ciudad o estado de la misma o que haya practicado la óptica en Puerto Rico por tres años con anterioridad al 31 de diciembre de 1968. No se admitirán diplomas de ópticos obtenidos mediante estudios por correspondencia.

3. Llenará, además, el solicitante, las formas suministradas por la Junta para acreditar, bajo juramento, la entidad genuina de los diplomas y títulos que posee. Los exámenes de reválida se efectuarán por escrito en el idioma español o inglés y cubrirá las materias pertinentes que decida la Junta. Además, se someterá a cada candidato a un examen práctico consistente en el manejo de aparatos e instrumentos empleados en la óptica.

Artículo 5.—La Junta Examinadora expedirá licencia de óptico a cualquier persona que haya solicitado a efecto con anterioridad al 31 de diciembre de 1969, pague los derechos correspondientes, apruebe un examen práctico y someta a la Junta evidencia que a su juicio sea satisfactoria, bajo juramento de ser mayor de 21 años de edad, ser ciudadano de los Estados Unidos, de buena conducta moral, que haya estado principalmente dedicado al ejercicio de la óptica en Puerto Rico a la fecha de su solicitud y durante un período de ocho años con anterioridad a la misma, o que ha terminado satisfactoriamente un curso de estudio de una escuela o colegio de óptica reconocida por la Junta, y obtenido el diploma correspondiente.

Artículo 6.—La Junta deberá cobrar los siguientes derechos:

$25.00 por cada examen

$10.00 por cada licencia original expedida

$10.00 por duplicado de una licencia extraviada o perdida

$25.00 por licencia expedida a los ópticos de cualquier estado de los Estados Unidos que mantenga acuerdos de reciprocidad con la Junta de Opticos de Puerto Rico.

Artículo 7.—Cancelación de Licencias

a) La Junta podrá revocar y cancelar la licencia de cualquier óptico en los casos siguientes:

1. Fraude o engaño durante el ejercicio de su profesión.
2. Haber sido declarado convicto de delito grave bajo las leyes de Puerto Rico o de cualquier estado de los Estados Unidos.
3. Ser un alcohólico consuetudinario o adicto a drogas narcóticas.
4. Incompetencia manifiesta en el ejercicio de su profesión.
5. Negociar u ofrecer la venta de una licencia para practicar la óptica.
6. Hacer cualquier testimonio falso en beneficio de un aspirante a examen ante la Junta Examinadora de Opticos.
7. Alterar cualquier documento o material con la intención maliciosa de que un aspirante sin tener la preparación o conocimiento necesario sea admitido a los exámenes de reválida u obtenga licencia para practicar.
8. Violación crasa a esta ley o sus reglamentos.

b) El procedimiento para estas revocaciones o cancelaciones será radicado ante la Junta siguiéndose el trámite establecido en los reglamentos que por éste se autorizan.

c) Las decisiones de la Junta serán revisables por el Tribunal Superior de Puerto Rico, Sala de San Juan, dentro de los treinta días siguientes a la notificación al interesado.

Artículo 8.—Convenio de Reciprocidad. La Junta Examinadora de Opticos de Puerto Rico tendrá facultad para conceder, mediante convenios de reciprocidad con estados de los Estados Unidos que exijan un alto grado de educación profesional, los mismos privilegios al conceder licencia sin examen.

Artículo 9.—Cláusula de Salvedad. Las disposiciones de esta ley no afectarán a los optómetras debidamente autorizados para ejercer su profesión en Puerto Rico.

Artículo 10.—Penalidades. Cualquier persona que directa o indirectamente se dedique al ejercicio de la óptica sin tener la

licencia correspondiente será convicto del delito menos grave y castigado con una pena de cárcel que no será mayor de un (1) mes de cárcel o multa no mayor de $500.00, o ambas penas a discreción del tribunal; disponiéndose, que en caso de reincidencia el delito aparejará un mínimo de treinta (30) días de cárcel, más la confiscación de todos los instrumentos y muebles utilizados en la práctica ilegal de la óptica.

Artículo 11.—Esta ley empezará a regir a los sesenta (60) días después de su aprobación.

NOTICIAS

HEW NEWS:

Changes in social security regulations to make them conform to a Supreme Court decision granting benefits to widowed fathers who have in their care children of their deceased wife, were published today by the Department of Health, Education, and Welfare.

The regulations implement the March 19, 1975 decision in Weinberger vs. Wiesenfield, in which the Court found unconstitutional the denial of benefits under the Social Security Act to widowers with children of their deceased spouse in their care while benefits were granted to widows under those circumstances. Under the new regulations, benefits are payable to either surviving parent.

An estimated 15,000 widowed fathers were made eligible immediately for social security benefits by the Supreme Court decision. The regulations, which establish March 1975 as the first month of eligibility for father's benefits, were published in today's Federal Register.

PUERTO RICO REGIONAL MEETING, American College of Physicians, Puerto Rico Medical Association Building and University of Puerto Rico School of Medicine, Río Piedras, Puerto Rico, Oct. 15-16, Info: José Torres-Gómez, MD, FACP, P. O. Box 2384, San Juan, P. R. 00903.

INTERNATIONAL DOCTORS IN ALCOHOLICS ANONYMOUS is a non-dues-paying organization of PHYSICIANS AND DENTISTS who get together at least yearly to help each other obtain and maintain their sobriety and freedom from drugs. The next annual convention will be held at the new LOS ANGELES MARRIOTT HOTEL, AUGUST 5 THROUGH 8, 1976. Tax deductible. Inquirers and newcomers welcome. For information write: Secretary, IDAA, 1950 Volney, Youngstown, Ohio 44511.

AMA NEWS:

PHYSICIANS SUPPORT CONTINUATION OF MEDICAID PROGRAM

CHICAGO – More than half of U. S. physicians polled by the American Medical Association say they support continuation of Medicaid – the federal government's program for financing medical care for the poor.

The problem facing doctors who did not give unanimous support is basic – government reimbursement for services often does not cover costs.

Results of the poll are published in the March 22 issue of American Medical News' monthly section on socio-economic issues of medicine, Impact.

Over three-fourths of the doctors polled declared, however, they would like to see modifications in the Medicaid program as now administered. A major objection cited is that reimbursement for medical services by the government is sometimes too low to cover costs.

So strong are physicians' feelings about Medicaid reimbursement levels and their inadequacy that four out of ten physicians said that unless fees are adjusted upward in 1976, they will see fewer Medicaid patients in the next 12 months.

In the same issue of American Medical News, Dr. Ralph Crawshaw, Oregon physician-writer, points out that in Portland the usual fee for a visit to a doctor's office is $10 to $12, of which about 60 percent goes for overhead. But Medicaid reimbursement to Oregon physicians for an office visit is pegged at $6.90.

Dr. Crawshaw declares that welfare recipients need first class medical care, that care of the indigent is often more difficult than treatment of patients who are economically self-sustaining, that those whose bills are paid by the government tend to over-utilize medical services. He suggests that the problem of over-utilization be met with a token payment required from the individual for each service rendered.

Impact also includes a report from an inner-city practitioner in Newark, N. J. who declares "I'm a Medicaid Doctor– and Proud of It." Dr. Edward A. Capriola describes his very busy practice as a pediatrician that is 90 to 95 percent children supported by Medicaid.

SEVENTH ANNUAL ASPEN RADIOLOGY CONFERENCE

The Seventh Annual Aspen Radiology Conference, designed for physicians and scientists interested in diagnostic radiology, nuclear radiology and diagnostic ultrasound, will explore the impact of clinical and technological advances on radiologic practice.

The Conference will be held February 28 to March 4, 1977 with registration Sunday, February 27 at the Aspen Institute for Humanistic Studies, Aspen, Colorado.

Further information may be obtained from Emanuel Salz-

man, MD, Conference Chairman, Division of Radiology, Beth Israel Hospital, Denver, Colorado, 80204. (303) 825-2190.

AMA NEWS RELEASE:

MEDICAL SCHOOLS URGED TO SEEK MORE SMALL TOWN STUDENTS

CHICAGO– Medical schools are urged to enroll more students from small towns and rural areas, and to step up training programs for family medicine, to produce more doctors that are likely to practice in rural areas, in a report in the Feb. 2 issue of the Journal of the American Medical Association.

Physicians with nonmetropolitan backgrounds are two to three times as likely to select nonmetropolitan practice as physicians with urban backgrounds, a study conducted by the University of Missouri School of Medicine at Columbia indicates.

And physicians who enter family medicine are almost three times as likely to select nonmetropolitan practice as physicians in other primary-care specialties.

A combination of these two factors results in two-thirds selecting rural or small town practice, the study shows.

While 26 percent of the nation's population lives in nonmetropolitan counties (those with no city having greater than 50,000 population), only 13 percent of the nation's physicians reside in these counties, says Sam Cullison, MD, and colleagues in the Missouri report.

Today, says Dr. Cullison, students with rural backgrounds are substantially underrepresented in the nation's medical schools. While 26 percent of the population live in nonmetropolitan counties, only 17 percent of entering medical students are from these counties.

However, studies show that the small-town student who specializes is much less likely to return to rural practice. Thus, the need for more medical school programs that stress preparation for family medicine.

UNSUPERVISED FASTING DANGEROUS TO HEALTH

CHICAGO– Unsupervised extended fasts to lose excess weight could do more harm than good to the unsuspecting dieter, says Philip L. White, Sc.D., director of the American Medical Association's Department of Foods and Nutrition.

In comment on a current popular diet book, "Fasting: The Ultimate Diet," by Allan Cott, MD. (Bantam Books, Inc., 1975) Dr. White declared that "Fasting for any extended period clearly requires careful medical supervision which cannot be provided from the pages of a book," Dr. Cott is now on the talk show circuit and excerpts of the book are appearing in newspapers and magazines, Dr. White said.

Dr. White's statement in American Medical News says:

"Dr. Cott, although warning of the advisability of medical sueprvision before embarking on a fast, reassures the reader about the ease, benefit and safety of fasting; thus encouraging fasts of months or more duration. The carrot on the stick is the promise of weight losses up to 20 percent of body weight in just four weeks. In his own words: 'Stunning weight losses during the first days – far exceeding those of even Dr. Stillman's socalled 'Water Diet' and Dr. Atkins' 'diet revolution' – are a powerful inducement to continue the fast.'

"While it is true that the obese individual is better able to tolerate fasting than is his lean counterpart (this may be the only advantage of obesity), the slightly overweight person or young woman preoccupied with slimness could be greatly harmed by a prolonged fast. Anorexia (loss of appetite) is an ever-present threat to overzealous young dieters because the large, initial weight losses may encourage prolonged fasting.

THE "PILL" NAMED AS CAUSE OF LIVER TUMORS

CHICAGO – Oral contraceptives may be the cause of tumors of the liver, a Kentucky research group report in the Feb. 16 issue of the Journal of the American Medical Association.

Doctors from the University of Louisville School of Medicine report on 13 young women who developed liver tumors after taking "The Pill." Nine of the tumors were benign, four were malignant. Six tumors ruptured spontaneously and caused life-threatening hemorrhage. Benign tumors were successfully removed by surgery in eight women. One woman died during surgery for a malignant growth.

"Primary tumors of the liver, previously rare among women in the United States, began to occur with increasing frequency after the introduction and widespread ingestion of contraceptive steroids," says surgeon E. Truman Mays, MD, and colleagues.

The patients were nonalcoholic, mostly young and generally healthy, and none had liver disease. The Pill causes substantial changes in the liver, he declares, pointing to impairment of the bile-secretory function in 10 to 40 percent of women taking the product.

ADVERTISING DETRIMENTAL TO QUALITY MEDICAL CARE

CHICAGO – Quality medical care cannot be mass-marketed at discount prices, declares W. R. Barclay, MD, editor of the Journal of the American Medical Association, in an editorial

in the Feb. 16 issue.

Dr. Barclay's editorial vigorously attacks an action of the Federal Trade Commission (FTC) in seeking to end the physician's traditional stand against solicitation of patients by advertising.

"The FTC contends that Madison Avenue hucksterism is the appropriate mechanism for establishing a patient-doctor relationship. The American Medical Association holds that medical need and professional competence should establish this relationship," Dr. Barclay writes.

"The competent physician does not advertise skill; it is self evident. The compassionate physician does not advertise compassion but practices it. Physicians bring compassion, skill and knowledge to their patients, and these are not commodities to be advertised in the newspaper or through television.

"The ethical physician will give needed care irrespective of the fee to be received. The services a physician provides are highly individualized and so should be the compensation for those services."

NEW ASTHMA DRUG PROVES EFFECTIVE, SAFE FOR CHILDREN

CHICAGO– A new drug product on the American scene has proved safe and effective in controlling asthma in children, says a research report in the Feb. 16 issue of the Journal of the American Medical Association.

The drug – metaproterenol sulfate – has the advantage of administration orally in a simple syrup mixture. It is available under trade names of Alupent and Metaprel.

Until recently the only orally administered asthma product available in the United States has been ephedrine sulfate, which had serious disadvantages, says Milan L. Brandon, MD, of the Allergy Medical Group of San Diego.

Dr. Brandon tested metaproterenol on a group of boys and girls age 6 to 13 years. Half of the group received the new drug; the other half were given a harmless placebo, or inert substance. None knew which substance he was receiving. The treatment of the 50 children was continued for three months.

The children taking the drug showed a distinct improvement in breathing when compared to those on the placebo. Side effects were minimal, he says.

AMA TO ESTABLISH COMMITTEE ON ETHICS

CHICAGO– A National Advisory Committee on Ethics will be set up by the American Medical Association in an effort to focus attention on the moral and ethical challenges facing American Institutions.

The AMA will help launch and finance the independently functioning committee, to be headed by Fred T. Allen, chairman of the Pitney Bowes Corp., Stamford, Conn.

"Our purpose," said Allen in a February issue of American Medical News, the AMA's weekly newspaper for doctors, "is to call attention to the importance of the ethical underspinning of business, law, medicine, journalism, education – in fact, our whole society. Without a pervasive pattern of individual honesty a free society cannot function.

"We are in an early development stage, just starting to approach people to participate. When we have formed a broadly representative group, then I think we can talk more specifically about our objectives and the means to attain them."

AMA President Max H. Parrott, MD, and Raymond T. Holden, MD, Chairman of the AMA Board of Trustees, said, "The AMA is initiating a National Advisory Committee on Ethics as a public service. The committee, its deliberations and its future recommendations will be independent of us.

CHAMPUS EXTENDS FY'76 DEDUCTIBLE CERTIFICATES TO SEPTEMBER 30

CHAMPUS beneficiaries will have three extra months this year before they must again satisfy the program's annual outpatient deductible.

Defense Department officials have announced that outpatient deductible certificates issued for Fiscal Year 1976 under the Civilian Health and Medical Program of the Uniformed Services (CHAMPUS) will be valid through September 30, 1976. During previous years, these certificates expired on June 30.

The one-time, three-month extension results from a realignment of the Federal Government's Fiscal Year. Previously, fiscal years began on July 1 and ran until June 30. Beginning this year, they will start on October 1 and end on September 30. The period from July 1 through September 30 was added to Fiscal Year 1976 to provide for the transition.

The outpatient deductible is the initial amount the beneficiary must pay each fiscal year before CHAMPUS assistance is available for outpatient expenses. For an individual, the deductible is the first $50 of authorized outpatient charges in a fiscal year. A family group of two or more is not required to pay collectively more than the first $100 of authorized outpatient charges in a fiscal year.

INTERSTATE SCIENTIFIC ASSEMBLY - November 15-18, 1976, Atlanta, Georgia

The 61st Annual International Scientific Assembly of Interstate Postgraduate Medical Association will be held at the Atlanta Marriott Hotel, November 15-18, 1976. This program is designed for Primary Care Physicians practicing in the U. S.

and Canada. It has been planned cooperatively with the Georgia Academy of Family Practice, the Emory University School of Medicine and the Medical College of Georgia. It provides 21 hours of PRESCRIBED and 3 ELECTIVE hours of credit for members of the American Academy of Family Physicians. A similar number of hours of credit toward the AMA Physicians's Recognition Award is provided through attendance.

The Assembly is open to any licensed physician in the U.S. and Canada at a fee of $50.00 in advance or $75.00 at the meeting. Those interested in the meeting and hotel forms should write to: Alton Ochsner, MD, Program Chairman, Interstate Postgraduate Medical Association, P. O. Box 1109, Madison, Wisconsin, 53701.

ANUNCIOS

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Para la venta - amplia oficina de aproximadamente 1079 pies. En Condominio Las Américas Professional colindante Hospital Los Maestros, al final Ave. Domenech. Sexto piso Núm. 608. Precio de ocasión, facilidades de pago. Inf.: Ing. R. Arce Preston, Tels. 767-1394, 723-6340.

VENDO

Oficina Ashford Medical Center - 600 pies, 8vo. piso, apartamiento en piso alto en Los Patricios y carro Vega 1974 equipado Dr R. A. Del Toro. Tels. 723-6225, 783-6051.

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Carbohydrate	12.8%	6.4%
Minerals (Ash)	0.9%	0.5%
Calcium	0.17%	0.085%
Phosphorous	0.13%	0.06%
Iron	0.002%	0.001%
Calories per fl. oz.	40	20

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Arthritic Doses

with more Maalox® to allow higher salicylate dosages, improved gastric tolerance.



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Drug Interaction Precaution: Do not use if patient is taking a tetracycline antibiotic.

Usual Adult Dose: Two or three tablets, four times daily, or as your physician directs for arthritis therapy. For children under twelve, consult a physician. If under medical care, do not take without consulting your physician.

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Continues to kill Staph. aureus and other burn wound invaders...

Furacin® soluble dressing
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With the constant advent of new antibacterials, resistance patterns change...but today, as in 1947, Furacin (nitrofurazone) continues to be bactericidal against *Staph. aureus,* the most common burn wound invader, and one which frequently develops resistance to other antibacterials. Furacin is also bactericidal against most other bacteria commonly causing surface infection.

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Contains: 0.2% Furacin (nitrofurazone). **Indications:** Adjunctive therapy for 2nd and 3rd degree burns when bacterial resistance to other agents is a real or potential problem. Skin grafting where bacterial contamination may cause graft rejection and/or donor site infections. **Contraindications:** Known prior sensitization to nitrofurazone. **Warnings:** Nitrofurazone has been shown to produce mammary tumors when fed at high doses to female Sprague-Dawley rats. The relevance of this to topical use in humans is unknown. *Safe use of nitrofurazone during pregnancy* has not been established. Use on women of child-bearing age is not recommended unless the therapeutic benefit outweighs the possible risk. **Precautions:** As with other topical antimicrobial agents, overgrowth of resistant organisms may occur. If this occurs, or if irritation, sensitization or superinfection develop, treatment with nitrofurazone should be discontinued and appropriate therapy instituted. **Adverse Reactions:** Furacin has not been significantly toxic in man by topical application. Sensitivity is low, with an overall incidence of 1.1 percent. Sensitivity reactions should be handled in a normal manner, except in the rare instance of severe contact dermatitis, when steroid administration may be indicated.

Boletín

asociación médica de puerto rico



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VOL. 68 AGOSTO 1976 NO. 8

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Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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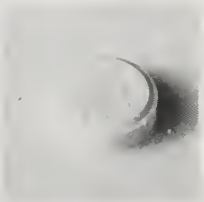
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respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium®
(diazepam) Ⓡ IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Today's woman can't hide an unsightly dermatosis, making effective treatment a necessity.

With its unique four-way action, Vioform®-Hydrocortisone provides the kind of comprehensive therapy that many common dermatoses* require, particularly those infected with fungi or bacteria.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.
If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.
Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE
Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED
Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. *Lotion*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

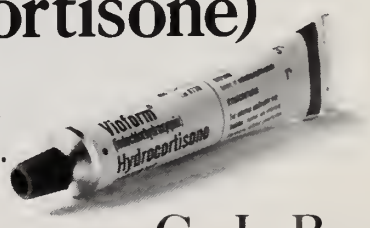
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BOLETIN ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial | Fundado en 1903 | Volumen 68 | Agosto 1976 | Número 8

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Second Class postage paid at San Juan, P. R.

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A SUMMARY OF BIOCHEMICAL CHANGES AND THE PATHOGENESIS OF LIVER COMA

Eduardo A. Santiago Delpín, MD, MS

From the very beginnings of recorded medical thought, the liver and its humors have been associated with the mind (44, 45, 54). Early physicians recognized the relationship of jaundice and delirium (19). These relationships were perhaps conclusively established by Frerichs who initiated the modern approach to liver disease through the publication of a monograph in 1860 (12). He described thirty-one cases of hepatic encephalopathy or "acholia" occurring in patients with cirrhosis or acute yellow atrophy of the liver. From then on we have a well-recognized entity.

Hepatic encephalopathy is defined as a disturbance in cerebral function associated with, and presumably due to, hepatic disease. Classically, the syndrome will include multi-system changes such as altered mental and neuromuscular state, liver stigmata, frequently raised blood and cerebrospinal fluid ammonia, abnormal biochemistries and an abnormal electroencephalogram (2, 5, 6, 9, 11, 15, 17, 25, 26, 27, 34, 35, 51-V, 60, 62, 63, 71, 73, 83, 88, 90, 101, 108, 115). The spectrum of the disease however, varies widely from patient to patient not only in severity, but also in mode of presentation, involvement of other organs and systems, and concommitant portal systemic shunting (62, 66).

The liver controls all the basic processes of life. Among its most important functions we include the metabolism of glucose, energy, ammonium, lipoproteins, proteins, amino-acids, fats, nucleic acids, toxins minerals, porphyrins, bilirubin, enzymes, hormones and vitamins (13), and the synthesis of protein, coagulation factors and urea.

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It is obvious that pathological derangements of such an organ will result in a vast array of biochemical abnormalities, which will not only vary with the severity of the pathologic process, but also with various extrinsic complicating factors, such as bleeding, diet and infection (95, 108, 117).

Metabolic Changes

Tables I-IV summarize most of the metabolic changes which have been described in liver failure with their pertinent references. We will highlight the more important changes, but the reader is referred to the tables for specific alterations.

Ammonia is still incriminated as the most likely agent responsible for the induction of hepatic coma (7, 15, 101, 108, 117), although this has been recently challenged (38-V). Evidence in favor of this hypothesis includes: a) patients with hepatic coma frequently have increased ammonia levels in blood and cerebrospinal fluid; b) coma may be precipitated in susceptible patients and animals by infusion of ammonia and substances giving rise to ammonia; c) frequent improvement by therapy directed at the removal of excess ammonia. Evidence against the role of ammonia includes: a) lack of precise correlation between the degree of neurologic impairment and actual ammonia levels; b) very high levels of ammonia are needed to induce coma in healthy experimental animals; c) the brain in hepatic coma does not always remove ammonia from the blood: on occasions it even adds to it; d) the lack of dramatic improvement in some patients in which ammonia is rapidly diminished.

Ammonia can be removed from the blood and tissues by one of three main mechanisms: the Krebs-Henseleit urea cycle, in which it combines with both ornithine and citruline forming arginine and giving rise to urea; the tricarboxilic acid cycle of Krebs, in which ammonia may bind to alpha-ketoglutaric acid yielding glutamic acid, which in turn, may bind more ammonia to yield glutamine; and the reaction with gammaaminobutyric acid to yield gammaguanidobu-

TABLE I
INCREASED METABOLITES IN LIVER COMA

Metabolite	Tissue or Fluid	Reference
1. NH_4^+	Blood, or C S F	16, 17, 19, 34, 60
2. NH_4^+, no coma	Blood	16, 55
3. Lactic Acid	Blood	12, 34, 49, 50, 52, 57, 61
4. p H	Blood	12, 44, 52, 58, 62
5. Pyruvate	Blood	12, 39, 49, 52, 61, 64
6. Serum Iron	Blood	49
7. Amino Acids	Blood	12, 49, 52, 70, 71, 72
8. Amino Acids	Urine	34, 49, 73, 74, 75, 76
9. Amino Acids	Brain	71
10. Amino Acids	C S F	49, 76, 77, 78
11. Sulfur Amino Acids	Body Fluids	80, 81, 82
12. Glutamine	Blood	19, 61, 83, 84, 85
13. Glutamine	Spinal Fluid	19, 61, 84, 85, 86
14. Alpha-Ketoglutarate	Blood	12, 39
15. Urocanic Acid	Urine	12
16. Glutamate	Blood	57
17. Acetoin (Pyruvate Deriv.)	Blood	64, 90
18. Butylene Glycol (Pyruvate Deriv.)	Blood	64, 90
19. Bilirubin	Blood	12, 49, 52, 53, 90, 91
20. Bile Salts	Blood	49
21. Bile Acids	Blood	92
22. Porphyrins	Blood & Urine	49
23. Fatty Acids (Short Chain; Even or Odd; Straight or Branched)	Blood	12, 76, 93, 94
24. Cholesterol	Blood	49
25. "Hormones"	Blood	49
26. Norepinephrine & Precursors	Brain	96
27. Norepinephrine	Brain	97
28. Serotonin	Brain	98
29. Arginase	Blood	104
30. Ornithine Transcarbamylase	Blood	50
31. Adenosine Deaminase	Blood	50
32. Transaminases	Blood	49
33. ALK. PTASE	Blood	49
34. Amino Peptidases	Liver	103
35. Serum Globulin	Blood	49
36. Protime	Blood	49, 52

tyric acid (81, 117). Bessman and Bessman originally theorized that a possible mechanism of ammonia toxicity could be through the drainage of alpha-ketoglutaric acid from the Kreb's cycle as described above. This would result in decreased aerobic metabolism of the brain (8). This hypothesis has been discussed extensive-

TABLE II
DECREASED METABOLITES IN LIVER COMA

Metabolite	Tissue or Fluid	Reference
1. P O 4	Blood	12, 43-A, 50
2. p H	Blood	63
3. pCO_2	Blood	12
4. K^+	Blood	12, 17, 44, 65, 66, 67, 68
5. Mg^{++}	Blood	12, 69
6. Blood Volume	Blood	70
7. Oxygen Consumption	Brain	12, 16
8. Cerebral Blood Flow	Brain	9
9. A-Ketoglutarate	Brain	45, 48, 61, 87, 88
10. Aspartic Acid	Brain	71
11. Cholesterol Esters	Blood	49
12. B-Complex Vitamins & Coenzymes	Blood & Liver	18, 95
13. VIT A	Blood	49
14. A T P	Cortex	99, 100
15. A T P	Brain Stem	87, 100
16. A T P - A S E	Blood	102
17. A D P - A S E	Blood	102
18. A M P - A S E	Blood	102
19. Phosphocreatine	Brain Stem	100
20. Phosphorylases	Liver	103
21. Arginase	Liver	104
22. Transketolase	Blood	18, 76
23. Transaminase	Blood	18, 76
24. Ribonucleotide Phosphohydrolase	Blood	105
25. Serum Proteins	Blood	49

TABLE III
UNCHANGED METABOLITES IN LIVER COMA

Metabolite	Tissue or Fluid	Reference
1. Amino Acids	Liver	79
2. Gamma-Amino-Butyric Acid	Blood, Brain	93
3. Norepinephrine	Besin	98
4. Serotonin	Brain	97
5. Acetylcholine	Brain	97
6. Cholinesterase	Blood	49, 101
7. Phosphocreatine	Cortex	100

TABLE IV
OTHER ALTERATIONS

Metabolite	Tissue or Fluid	Reference
1. Need for Cytidine & Uridine	Brain	89
2. "Disturbance of Phenols & Indoles"	Blood	45

ly in the literature, and even if complete proof is lacking, it is extremely appealing. It is consonant with the observations of a decreased glucose utilization of the brain, a decrease in its oxygen consumption (38, 117), the decrease in brain alpha-ketoglutaric acid found by some investigators (7, 19, 97), and the increase in brain and CSF glutamine (17, 95, 102, 105, 114). Severe demands are thus presumably imposed on the glycolytic pathway which is already handicapped by a diminished reserve of such co-factors as vitamins (4) and magnesium (10). Another detrimental result may be a decrease in available reduced diphosphopyridine nucleotide because of its consumption in converting alpha-ketoglutaric acid to glutamate rather than in providing electrons for respiration. In addition, the ATP (adenosine triphosphate) yield of anaerobic glycolysis is much less than that of the regular oxidative pathways, and since ninety percent of the brain metabolism is aerobic, anaerobic conditions will cause brain malfunction.

A specific selectivity in some of these changes seems to reside in the brain stem as shown by the more marked chemical changes in this region (92, 97). These findings are not incompatible with the fact that asterixis and decerebrate rigidity are abnormalities that to a large extent arise in the brain stem. Also, hyperpnea may result from a disfunction of the respiratory center giving rise to the respiratory alkalosis frequently seen. Coma itself probably results from impaired transmission of exogenous stimuli to the brain stem and reticular formation and thence to the cortex. From these considerations, it has seemed reasonable to conclude that reduced cellular oxidative metabolism is fundamental in liver coma (91-A).

Even though this theory is appealing and explains many observations, there are other biochemical changes which complicate the picture (58). Short chain fatty acids have been shown to produce a syndrome very similar to hepatic coma in clinical as well as in EEG characteristics (76, 89, 118). Conversely, fatty acids are also frequently elevated in patients with liver coma (100). The mechanism of action is not known, but a direct toxic action on the brain or synaptic transmission may be postulated.

Another line of current investigation is that of neurotransmitters. Norepinephrine, serotonin, and possibly histamine may be also involved in neurohumoral synaptic transmission (38). Presumably, in liver failure or portosystemic shunting, amines produced in the gut by decarboxylation bypass the liver and flood the CNS releasing and replacing the normal endogenous transmitters, thus acting as false neurotransmitters (38-A). Electrical neurotransmission is in effect weaker and abnormal. Some investigators (85) have shown that there is a significant increase in whole brain concentrations of norepinephrine and its metabolic precursors, phenylalanine and tyrosine, suggesting an increased intracerebral synthesis of nor-epinephrine, whereas others have shown normal levels in cerebral cortex and brain stem (112). The fact that Parkes (82) and Fisher (38-A, 39, 87) have successfully reverted patients in hepatic coma with L-DOPA, (L-deoxyphenylalanine), gives weight to the role of neurotransmitters in this syndrome.

The role of gamma-aminobutyric acid must also be considered. This acid is formed by the decarboxylation of glutamate and supposedly is an inhibitory factor in the brain (36) although some investigators have questioned this effect (50, 82, 86). It blocks the synaptic transmission in gangliae and in the spinal cord. It diminishes the response of the brain if utilized topically. However, its content during liver coma has not been specifically measured and there does not seem to be any specific reason why glutamate would choose to follow decarboxylation rather than amination into glutamine (other than providing a substrate for further amination into gamma guanidobutyric acid).

An additional complicating factor seen in acute liver failure, consists of postulating a direct toxic action of some of the enzyme and vasoactive peptides which are spilled during liver necrosis. This may explain the blood volume and pressure changes usually seen in acute cases, as well as the changes in distribution of blood flow. However, this particular problem is much more complex, and may not have direct bearing on the changes seen in the chronic forms (28).

Additional Theoretical Considerations:

Figure 1 summarizes some of the more important changes described, translated into the general scheme of intermediary metabolism. As the central item we see the tricarboxylic acid cycle of Krebs. To this central cycle converges the intermediary metabolism of glucose after its reduction to pyruvate. Fatty acids converge as acetyl-CoA. After transamination or deamination, amino acids also enter with CoA into the cycle. Careful consideration of these findings shows that a lack of CoA can probably result in most of the described changes. It can explain the elevation of fatty acids, which can only be metabolized with CoA during beta oxidation (117). It also explains why we have accumulation of toxic metabolytes from glucose metabolism, since they result from the alternate pathway followed when pyruvate cannot enter the cycle if Coenzyme-A is absent. It explains a possible decrease in acetylcholine since this is formed from active acetate and choline. The accumulation of most amino acids is also explained, as is the presence of toxic amines including false neurotransmitters which result from decarboxilation of amino acids rather than the usual pathway with CoA which is now blocked.

However, why the decrease of CoA? CoA is formed from the vitamin pantothenic acid, cysteine and ATP. We could postulate either a decrease in any of the three reactants, or blockage of the metabolic reactions among themselves. A decrease in ATP (91, 92, 97) has been observed, and may be explained on the basis of a chronic drain from important cellular maneuvers into reactions which enhance the removal of ammonia. The second possibility would be a depression of pantothenic acid itself since most vitamins are decreased (4, 66). Non-specific neurologic and psychiatric changes have been described by blocking pantothenic acid in human volunteers (55). Blockage by ammonia of the enzyme systems involved in these reactions is conceivable.

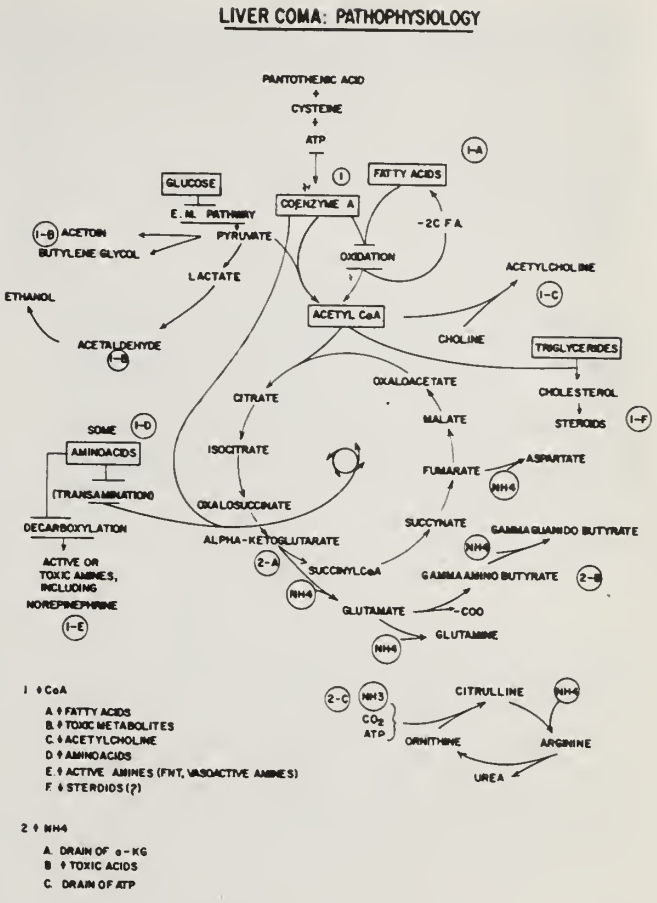


Fig. 1: *A schematic presentation of the convergence of the three main food stuffs, carbohydrates, fats and amino acids, into their common final energy pathway. Ammonia metabolism is also incorporated.*

An objection raised to this concept is the failure of CoA infusion to revert the syndrome of hepatic coma (18, 107). However, since CoA passes the cell membrane only with difficulty (33), intravenous infusion of the substance cannot be equated with its availability inside the cell. In order to prove or disprove this objection we would have to make CoA available to the cell by altering its relative membrane permeability.

Summary

The liver controls all the basic processes of life. Since its most important functions include the metabolism of glucose, energy, proteins, coagulation factors, lipids, amino-acids, nucleic acids, toxins, enzy-

mes, hormones, and vitamins, it is obvious that derangements of this organ will be manifested by changes in the chemical environment of the different body fluids. No less than 70 changes have been reported in the literature in the various tissues and fluids, and these are presented in tabular form together with the more important references.

Even though ammonia is currently considered as the most likely agent responsible for the induction of hepatic coma, other current theories are discussed. These include the role of neurotransmitters (acetylcholine, epinephrine, norepinephrine) false neurotransmitters, gamma-aminobutyric acid, lipids, and finally, some theoretical considerations on the central role of Coenzyme-A and ATP.

Acknowledgment

The author recognizes the excellent secretarial assistance of Ms. Laura Mercado.

References

(A full reference list will be mailed upon request.)

EL SINDROME DE PRE-EXCITACION EN PEDIATRIA
Consideraciones Clínicas y Terapéuticas

Jorge Sánchez, MD
Mercedes Vega Vidal, MD
Felipe Vizcarrondo, MD
Agustín Muñoz, MD
Amalia Martínez Picó, MD

El síndrome de pre-excitación originalmente descrito por Wolff, Parkinson y White (1), se caracteriza por sus hallazgos electrocardiográficos y clínicos. Los primeros se deben a la excitación temprana de los ventrículos por una transmisión anormal del impulso eléctrico que se propaga desde los atrios usando una conección aberrante; esto se manifiesta en el electrocardiograma por un PR corto, un complejo QRS ancho provisto de una onda delta y cambios en la onda T y el segmento ST. Las manifestaciones clínicas se refieren a la presencia de taquicardia paroxística que a veces crean problemas para los pacientes (2-3).

Los avances obtenidos en años recientes sobre la electrofisiología, farmacología y terapéutica de esta entidad, han renovado el interés por su mayor conocimiento y mejor manejo de los pacientes portadores de pre-excitación. Aunque se piensa que el pronóstico a largo plazo en la mayoría de los niños es benigno (4), se realizó el presente estudio con el propósito de evaluar los pacientes y sentar pautas para manejarlos de acuerdo a los últimos adelantos diagnósticos y terapéuticos con que se cuentan actualmente.

Material y Métodos

El estudio consta de 20 infantes y niños de 12 años de edad o menores con pre-excitación tratados en la Sección de Cardiología Pediátrica del Hospital Universitario de San Juan, Puerto Rico. Doce de los pacientes son varones. La edad en que se hizo el diagnóstico varía desde las dos semanas hasta los nueve años, siendo 15 de ellos menores de dos años. Los períodos de seguimiento son los siguientes: seis a doce meses en dos pacientes, de uno a cinco años en nueve pacientes, de cinco a 10 años en seis pacientes y tres tienen más de 10 años de seguimiento (Tabla I).

De la Sección de Cardiología Pediátrica, Departamento de Pediatría, Escuela de Medicina, Universidad de Puerto Rico.

Todos los pacientes tienen exámenes clínicos, radiografía de tórax, electrocardiograma y vectocardiograma. En casos de cardiopatía congénita asociada se realizaron además cateterismo cardíaco y/o cirugía.

El diagnóstico de pre-excitación se realizó por los hallazgos electrocardiográficos de un intervalo PR igual o menor a 0.08 segundos en recién nacidos y de 0.10 segundos o menos durante el resto de la edad pediátrica. El complejo QRS ancho y provisto de una onda delta con una duración mayor de 0.07 segundos en recién nacidos y de más de 0.09 segundos en niños mayores (5).

Cuando el QRS y la onda delta fueron predominantemente positivos en las derivaciones precordiales se les clasificó en el tipo A (Fig. 1) y cuando las deflecciones fueron mayormente negativas en las precordiales derechas se les agrupó en el tipo B (Fig. 2). También se realizaron mediciones durante trazados normales en aquellos con la variedad intermitente. El diagnóstico de taquicardia paroxística supraventricular se realizó identificando la onda P con su correspondiente QRS (Fig. 3).

Resultados

La distribución por sexo demuestra una ligera predominancia de los varones (60 por ciento). En ninguno existe historia familiar. La mayor parte (75 por ciento) se diagnosticaron en la infancia.

Los pacientes fueron clasificados de acuerdo a sus manifestaciones clínicas en tres grupos, (Tabla II).

1. *Grupo Asintomático:* Comprende cinco pacientes (25 por ciento), tres del tipo B y uno del tipo A, en ellos el problema de conducción fue un hallazgo coincidental durante una evaluación cardiovascular y se mantuvieron asintomáticos a lo largo del seguimiento.

II. Grupo Sintomático: Consta de 11 pacientes (55 por ciento) con paroxismos de taquicardia supraventricular causados exclusivamente por el trastorno eléctrico. Tres pacientes con tipo B de pre-excitación presentaron palpitaciones y mareos que aunque no probados electrocardiográficamente los atribuímos por el historial a episodios de taquicardia (subgrupo a). La arritmia se pudo documentar por medio del electrocardiograma en ocho pacientes (subgrupo b), cuatro

TABLA I - DATOS GENERALES Y PERIODOS DE SEGUIMIENTO EN LOS VEINTE PACIENTES

DATOS GENERALES EN 20 PACIENTES

Sexo	varones	12
	femenino	8
Edad al diagnóstico:	2 semanas a 9 años (15 infantes)	
Años de seguimiento:	6 a 12 meses	2
	1 a 5 años	9
	5 a 10 años	6
	mas de 10 años	3

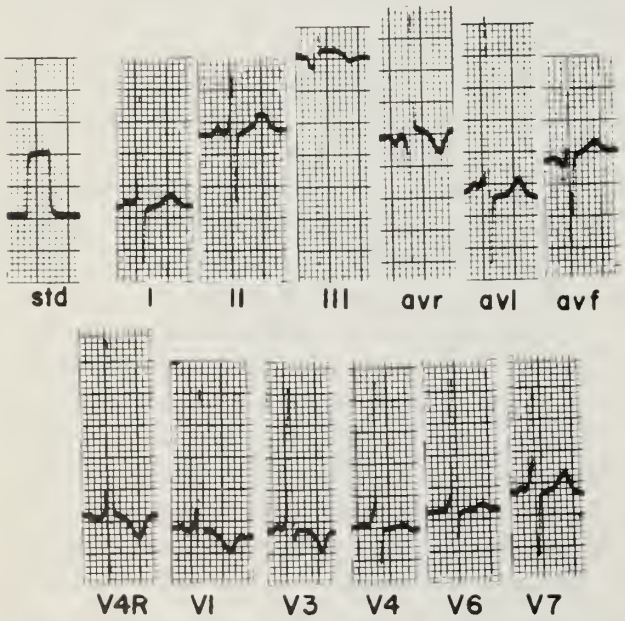


Figura 1: *Electrocardiograma con el tipo A de pre-excitación mostrando un P-R corto y un QRS predominantemente positivo en las derivaciones precordiales.*

TABLA II - GRUPOS CLINICOS EN LOS CUALES FUERON AGRUPADOS LOS PACIENTES DE ACUERDO A SU FORMA DE PRESENTACION

I -- Pacientes asintomáticos	5
II -- Pacientes sintomáticos	11
a- mareos y palpitaciones	
b- taquicardia paroxística documentada	
c- arritmia complicada con insuficiencia cardiaca	
III - Pacientes con cardiopatía asociada	4

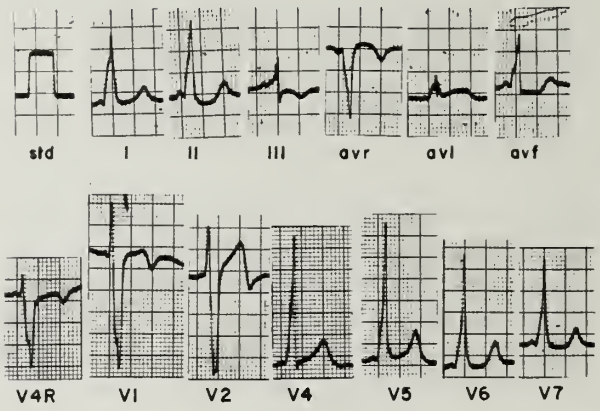


Figura 2: *Electrocardiograma con el tipo B de pre-excitación en el cual las deflecciones del QRS son predominantemente negativas en las derivaciones precordiales derechas.*

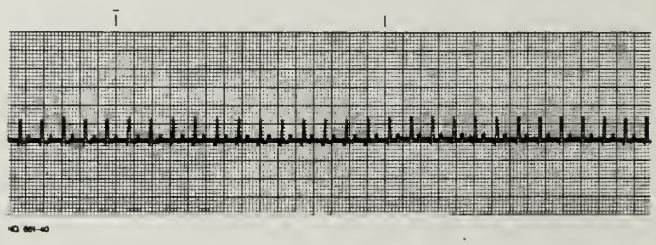


Figura 3: *Trazado largo de derivación II que demuestra taquicardia paroxística supraventricular.*

del tipo A y cuatro del tipo B. Este grupo presentó la variedad intermitente en tres pacientes y se complicó frecuentemente con insuficiencia cardíaca (subgrupo c).

Taquicardia paroxística supraventricular: La presencia de esta arritmia tuvo las siguientes características:

1. Siete de ocho pacientes se complicaron con insuficiencia cardíaca; todos ellos menos uno eran infantes.
2. La insuficiencia cardíaca se presentó más rápidamente cuanto menor la edad y mayor la respuesta ventricular de la taquicardia.
3. La arritmia fue desencadenada por infecciones respiratorias en cuatro de los ocho pacientes por ansiedad o ejercicio en dos de ellos (Tabla III).
4. La duración de la arritmia varió desde pocos minutos en un paciente hasta cuatro días en otro, éste representó la duración más larga.
5. Cuatro pacientes tuvieron que admitirse al hospital para el control de la arritmia, todos ellos permanecieron menos de una semana.
6. En todos los casos excepto uno se usó la digital para controlar los episodios, en el caso restante fue necesario agregar quinidina.
7. En cuanto a las recidivas, un infante tuvo seis episodios en el primer año de vida, siguen en orden de frecuencia episodios de cinco por año hasta llegar a un paciente que sólo presentó un episodio.
8. Una vez que los pacientes dejaron de ser infantes con tratamiento adecuado desapareció la taquicardia en tres y se espaciaron los paroxismos a dos por año o menos en el resto.
9. Un paciente sigue presentando mareos cuando deja de tomar la digital.
10. Dos pacientes complicados con insuficiencia cardíaca normalizaron su electrocardiograma, uno a los tres meses y el otro a los seis años de edad. El trazado ha permanecido normal, comprendiendo tres años de seguimiento para el primer caso y cinco años para el segundo.
11. El análisis electrocardiográfico de la taquicardia supraventricular demostró una variación en la frecuencia desde 200 hasta 320 por minuto. En todos ellos se normalizó el QRS y desapareció la onda delta.
12. Siete pacientes presentaron en el electrocardiograma la onda P precediendo el QRS durante la taquicardia paroxística, en un paciente la onda P seguía al QRS (taquicardia reciprocante).

TABLA III - FACTORES DESENCADENANTES DE LA TAQUICARDIA PAROXISTICA SUPRAVENTRICULAR

FACTORES DESENCADENANTES DE TPS
Fiebre
Infecciones respiratorias
Ansiedad
Ejercicio

TABLA IV - VARIEDADES DE CARDIOPATIAS ASOCIADAS AL SINDROME DE PRE-EXCITACION

GRUPO ASOCIADO A CARDIOPATIA CONGENITA
Comunicación interventricular
Anomalía de Ebstein
Coartación aórtica con Conducto Arterioso

* Ninguno presentó arritmia

III.Grupo Asociado a Cardiopatía Congénita: Comprende cuatro pacientes: uno con comunicación interventricular y pre-excitación del tipo A, otro con anomalía de Ebstein y pre-excitación del tipo B. El tercero es un infante con coartación de la aorta y persistencia del conducto arterioso, que se presentó con insuficiencia cardíaca y pre-excitación del tipo B. Fue cateterizado y operado con éxito en el período neonatal. El cuarto tenía el tipo B intermitente asociado a una coartación aórtica corregida a la edad de seis años. Ninguno de estos pacientes que constituye el 16 por ciento del material presentó episodios de taquicardia (Tabla IV).

Discusión

La importancia clínica del síndrome de pre-excitación estriba en la presencia de episodios de taquiarritmia. Generalmente se trata de taquicardia paroxística supraventricular, pero puede ocasionalmente ser fibrilación atrial y hasta taquicardia ventricular. Estos ritmos rápidos constituyen una sobrecarga tanto para un corazón sano, como para uno afectado por una cardiopatía (6). La severidad de esta sobrecarga es variable, puede resultar intolerable en un infante con una cardiopatía severa, ser mejor tolerada en otro paciente con corazón morfológicamente normal y hasta pasar desapercibida en un niño mayor. La sobrecarga es más peligrosa cuanto menor sea la edad del paciente, mayor la frecuencia ventricular y más severa la cardiopatía.

Nuestro grupo de pacientes tuvo un pronóstico benigno ya que no tiene mortalidad y la arritmia fue controlada fácilmente; la edad de cuidado fue la de la infancia y ninguno de los pacientes con cardiopatía asociada se complicó con episodios de arritmia. Otras series sin embargo no son tan afortunadas ya que tienen mortalidad (4) o dificultades en el control de la arritmia, como el caso de Dreifus (7) que requirió la implantación de un marcapaso.

El manejo adecuado de pacientes pediátricos con pre-excitación debe basarse en dos factores importantes: la edad y el grupo clínico al que pertenecen.

La edad infantil es la de mayor cuidado ya que el pronóstico mejora notablemente después de la infancia.

Los pacientes del primer grupo quienes se han mantenido asintomáticos requieren solo evaluaciones cardiológicas, con el objeto de descubrir la aparición de episodios de arritmia y de observar cambios en el trazado electrocardiográfico.

El grupo sintomático que padece de mareos y palpitaciones atribuídos a episodios de arritmia (subgrupo A) puede complicarse ocasionalmente con convulsiones o ataques de Stokes-Adams (2, 8). En ellos es importante documentar electrocardiográficamente la arritmia para evitarle al paciente procedimientos diagnósticos tendientes a explicar las manifestaciones clínicas. Tres pasos son importantes en el manejo de estos pacientes: 1) prevenir los factores precipitantes que pueden ser la fiebre, la ansiedad o el ejercicio extenuante, 2) evitar actividades potencialmente peligrosas como el nadar solos o situarse en lugares altos desde donde pueden sufrir caídas y 3) abolir los episodios por medio del agente farmacológico apropiado (Tabla V).

En los pacientes con episodios comprobados de taquicardia supraventricular (subgrupo B) es importante interrumpir la arritmia especialmente en infantes o en cardiópatas ya que pueden complicarse fácilmente con insuficiencia cardíaca o empeorarse una ya existente. El éxito obtenido en nuestra serie y en la de otros autores (4, 9) con la digital nos permite aconsejarla como fármaco inicial en las dosis recomendadas por Nadas (9). La digital interrumpe el movimiento circular que es el responsable de perpetuar la arritmia. Esta interrupción se debe a la prolongación del período refractario del nódulo atrioventricular (10). La quinidina, usada en otros casos actuaría prolongando el período refractario del puente aberrante. Sin embargo de parecer lógica esta explicación no se aplica en todos los casos debido a la complejidad anatómica y electrofisiológica de estas estructuras (5, 11, 12, 13, 14). Aunque nuestra experiencia está limitada a la digital y a la quinidina, se pueden usar otros fármacos como la procainamida o la difenilhidantoína. En otros casos más difíciles será necesario emplear procedimientos tales como la cardioversión (15) y la inserción de marcapasos (7).

Tan importante como el control de la taquiarritmia es la prevención de las recidivas; afortunadamente la mayoría se controlan usando los fármacos mencionados y evitando los factores precipitantes. Un número muy reducido requerirá medidas más drásticas que incluyen: la inserción de marcapaso permanente (7), la sección quirúrgica del haz aberrante (16), o la creación de un bloqueo atrioventricular completo seguido por la implantación de un marcapaso permanente (17). Entendemos que estas dos últimas medidas no se han realizado

TABLA V - MANEJO DE PACIENTES CON MAREOS O PALPITACIONES

MANEJO DE PACIENTES CON MAREOS O PALPITACIONES

1- Prevenir factores precipitantes: fiebre, ansiedad
2- Evitar actividades peligrosas: nadar
3- Abolir la arritmia por los medios adecuados

en niños, gracias al control de la arritmia por medios más simples. En cuanto a la sección quirúrgica del haz aberrante, ésta fue posible gracias a la obtención de diagramas eléctricos del epicardio iniciados por Durrer (18) y al reporte de Cobb (16) concerniente a un caso tratado existosamente por la cirugía. Las indicaciones para este tipo de tratamiento son rigurosas, se reservan para casos que no responden a medidas menos cruentas y están numeradas por Narula (19). Para que la cirugía sea existosa es necesario localizar con precisión el puente aberrante, esto exige una exploración electrofisiológica completa que además del electro y vectocardiograma, incluye procedimientos sofisticados tales como: trazados intracavitarios, electrocardiograma del haz de His, estimulación intracardíaca por marcapaso externo y finalmente, ya al tiempo de la cirugía, el diagrama eléctrico epicárdico.

El hecho de que no todos los pacientes se beneficien de la cirugía se debe a que pueden existir conecciones múltiples, o que éstas se encuentran muy cerca del sistema de conducción normal. Generalmente los afortunados han sido los portadores del tipo B de pre-excitación, aunque recientemente se ha reportado éxito quirúrgico en pacientes con pre-excitación del tipo A y también en aquellos con conecciones muy cercanas al septo (14, 20, 21, 22).

En contraste con estos pacientes que son refractarios al tratamiento, existen otros que se curan espontáneamente como ocurrió con dos de nuestros casos que normalizaron su trazado electrocardiográfico, uno a los tres meses de edad y el otro a los seis años. Es posible que en el infante la maduración del sistema de conducción no se haya completado al nacimiento, sino como opina James (22) haya requerido varios meses para hacerlo. En el paciente de seis años probablemente se debió a un bloqueo del haz aberrante, mecanismo que nos parece el más lógico entre todos los indicados por Massumi (23).

El grupo que tiene la asociación de pre-excitación y cardiopatías es más complejo. La variedad de cardiopatías asociadas al problema eléctrico es muy amplia (2, 24), la mayor parte son congénitas pero también las hay adquiridas. Para tratar adecuadamente a estos pacientes es necesario conocerlos tanto electrofisiológica como hemodinámicamente. Esto permitirá controlar la arritmia sin empeorar las alteraciones producidas por la cardiopatía y viceversa, manejar la cardiopatía sin provocar episodios de taquicardia. Cuando la cardiopatía requiere tratamiento quirúrgico habría que tener en mente el seccionar al mismo tiempo la conección aberrante, siempre que sea técnicamente posible y que así esté indicado hacerlo. Esperamos que con mejores métodos de diagnóstico el número de pacientes beneficiados vaya en aumento.

La única ventaja imaginable y digna de explorarse de la asociación entre cardiopatía y pre-excitación la tendrían aquellos pacientes con bloqueos atrioventriculares completos post-quirúrgicos. Ellos podrían usar esta conección accesoria para su conducción atrioventricular y evitar un marcapaso permanente que tantos problemas ofrece en la edad pediátrica (25). El caso reportado por Timmis (26) demuestra esta posibilidad.

Todos los adelantos recientes descritos en la literatura referentes al diagnóstico y tratamiento del síndrome de pre-excitación y la revisión de nuestro material a través de los años, nos indican que el manejo adecuado de estos pacientes debe individualizarse teniendo en cuenta su edad y el grupo clínico al que pertenecen. El determinar la variedad electrofisiológica es importante para localizar las conecciones aberrantes que uno intenta abolir con los diferentes medios terapéuticos.

A pesar de que este síndrome ha sido extensamente estudiado en todos sus aspectos desde su descripción original en 1930, pensamos que seguirá fascinando tanto a clínicos como a electrofisiólogos por mucho tiempo.

Resumen

Se describen 20 casos pediátricos con pre-excitación seguidos por períodos variables de tiempo.

Los cuales se dividen en 3 grupos:

I- Grupo asintomático que se mantuvo sin manifestaciones clínicas durante el seguimiento, requiriendo solo evaluaciones infrecuentes.

II. Grupo sintomático con episodios de taquiarritmia, la mayoría de ellos infantes y complicados con insuficiencia cardíaca, quienes respondieron bien a la digital. Algunos pacientes en este grupo presentaron palpitaciones y mareos.

III. Grupo asociado a cardiopatías congénitas tales como defecto interventricular, anomalía de Ebstein y coartación aórtica con conducto arterioso. Ninguno presentó taquiarritmia.

Se indica que el pronóstico y el manejo dependen de la edad y del grupo clínico. Se discute el tratamiento utilizado en cada grupo y el existente para casos refractarios. Se enfatiza que el plan de manejo debe

ser individual teniendo en cuenta, edad, grupo clínico y variedad electrofisiológica.

Summary

Twenty pediatric patients with pre-excitation syndrome followed up for variable lengths of time were reviewed. They were divided in three groups:

Group I - Asymptomatic patients who remained without symptoms throughout the follow up and required only infrequent cardiovascular evaluations.

Group II- Symptomatic patients, most of them infants presenting with tachyarrhythmia, complicated with heart failure and treated successfully with digitalis. A few patients in this group presented with palpitations and dizzy spells.

Group III- Includes patients who have associated congenital heart disease, such as ventricular septal defect, Ebstein disease and coarctation of the aorta with patent ductus arteriosus. None of them presented with tachyarrhythmias.

Emphasis is made on the fact that prognosis and adequate management depend upon the age and the group to which the patient belongs. Appropriate treatment for mild and refractory cases is discussed. This should be individualized taking into consideration the patient's age, clinical and electrophysiological variety.

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FISTULA ARTERIOVENOSA PULMONAR: REPORTE DE UN CASO

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Desde el informe inicial de Churton (1) en 1897, el síndrome clínico de fístulas arteriovenosas pulmonares está siendo reconocido cada vez más como entidad clínica. En 1917, Wilkins (12) correlacionó los hallazgos anatómicos con la sintomatología clínica. Smith y Horton (10) hicieron en 1939 por primera vez el diagnóstico de esta condición en un sujeto vivo. No fue hasta 1942 que Hepburn y Dauphinee (5) describieron la cirugía curativa para una fístula arteriovenosa pulmonar. Desde entonces, se ha descrito un número definido de casos con esta anomalía.

Aquí trataremos de una fístula arteriovenosa pulmonar en un joven de 18 años, quien fue examinado y tratado en el Hospital Universitario del Centro Médico de Puerto Rico. Nuestro propósito es repasar el tema de las fístulas arteriovenosas y presentar, al mismo tiempo, los estudios radiográficos del paciente.

El caso es como sigue: Este adolescente fue referido al Hospital Universitario en 1959 por estar sufriendo de cianosis de las mucosas y de un desarrollo físico tardío. Durante la evaluación del paciente se le encontró un soplo sistólico en el borde esternal izquierdo y un soplo contínuo en el hemitórax derecho. La angiografía pulmonar demostró la presencia de una fístula arteriovenosa pulmonar en el lóbulo inferior derecho. Un año más tarde, en 1960, se le practicó una lobectomía, mejorando así los síntomas hasta el punto de considerarse curado al joven. No se volvió a saber de él hasta 1968 en que fue nuevamente referido a nuestro hospital, debido a que había desarrollado movimientos tónico-clónicos de tipo gran mal. Se le estudió minuciosamente desde el punto de vista neurológico, practicándosele escintigrama de cerebro, electroencefalograma y estudios radiográficos en la cabeza, sin que se pudiera identificar patología orgánica para explicar las convulsiones.

En septiembre de 1975, el paciente vuelve a nosotros quejándose de cansancio al esfuerzo y cianosis, negando ortopnea, disnea en descanso, edema de las extremidades, hemotisis, hematuria o sangría gastrointestinal. No existía historial familiar de condiciones similares.



Figura 1

Del Departamento de Medicina, Hospital Universitario, Universidad de Puerto Rico.

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TABLA I
PRUEBA DE FUNCION PULMONAR

	Normal	Paciente
VC	4,455 ml	3,808 ml
FRC	3,740 ml	3,309 ml
TLC	6,530 ml	5,426 ml
FEV_1	3.4 lt/sec	3.2 lt/sec
MMEFR	3.5 lt/sec	3.72 lt/sec
DLco	16.9 ml/min/mmHg	23.5 ml/min/mmHg

TABLA II
GASES ARTERIALES

	Aire	100 °/o O_2 X 20 min.	100 °/o O_2 X 40 Min.
pH	7.43	7.41	7.40
pO_2	52	99	109
pCO_2	32	35	35.5
Hb	18.4	18.4	18.4
Base	-2		
HCO_3-	21		

El examen físico reveló un pulso regular de 84 por minuto; una presión arterial de 110/70; frecuencia respiratoria de 16 por minuto; cianosis en los labios y en los dedos que semejaban palillos de tambor; una cicatriz en el hemitórax derecho que evidenciaba la cirugía anterior; corazón de tamaño normal pero con un soplo sistólico grado 4/6 en el borde esternal izquierdo que irradiaba la base y a la punta del corazón: variación del soplo con la respiración haciéndose más fuerte con la inspiración profunda; los pulsos periféricos normales; no había edema de las extremidades inferiores; el examen neurológico era esencialmente negativo; la hemoglobina era de 18.8 gramos, y el electrocardiograma era normal pero tenía un eje derecho de +105 grados; la radiografía del tórax (figura 1) señalaba cambios fibróticos en el lóbulo inferior derecho como resultado de la cirugía previa; un corazón de tamaño normal, y una masa lobulada grande cerca del hilio izquierdo.

Las pruebas de función pulmonar (Tabla I) y las pruebas de gases arteriales (Tabla II) demostraban una hipoxemia severa que corregía pobremente al inhalar oxígeno al 100 por ciento. El cortocircuito de sangre era de aproximadamente 30 por ciento. La angiografía pulmonar (Fig. 2) tenía una fístula arteriovenosa pulmonar en el hilio izquierdo. Tomando en cuenta el tamaño y posición de la anomalía, se decidió observar al paciente, ya que la cirugía era muy arriesgada en este caso.

Comentarios

Comentando el caso, diríamos que las fístulas ar-



Figura 2

teriovenosas pulmonares pueden ser congénitas o adquiridas. Usualmente, las congénitas no aparecen hasta la segunda o tercera década del paciente, pero se han dado casos en la infancia y en los envejecientes (11). Se cree que las fístulas congénitas crecen gradualmente como resultado de la debilidad en la pared venosa ante la presión ejercida por el torrente sanguíneo arterial. Estas fístulas arteriovenosas se encuentran como lesiones solitarias o múltiples, unilaterales o bilaterales, pequeñas o grandes. Lo más frecuente es que la comunicación sea de arteria pulmonar a vena pulmonar. No obstante, se han descrito casos raros donde la comunicación es de arteria pulmonar al atrio izquierdo (3) o de arteria intercostal a vena pulmonar, haciendo un cortocircuito sistémico pulmonar (2). Las fístulas arteriovenosas pulmonares adquiridas están asociadas a entidades tan dispares como carcinoma metastático de tiroide (9) cirrosis hepática de larga duración, esquistosomiasis (7) y a trauma (2). Sin embargo, el origen y la patofisiología de las fístulas adquiridas está aún por descifrarse.

Las manifestaciones clínicas más frecuentemente asociadas a esta condición son: cianosis, disnea al esfuerzo y dedos en forma de palillos de tambor. La sintomatología de la condición dependerá del tamaño del cortocircuito sanguíneo en la lesión. En la gran mayoría de los casos, el volumen es suficiente para causar cianosis, pero no lo bastante para producir disturbios hemodinámicos que comprometan la función cardíaca (8). Otros síntomas incluyen: debilidad, mareos, desmayos, diplopia, dolor de pecho, policitemia, epístaxis, hematemesis y sangría por los labios u otras superficies mucosas. En el examen físico casi siempre se oye un soplo contínuo sobre el área de la anomalía, oyéndose mejor en la inspiración profunda. En ocasiones el soplo puede desaparecer en la expiración.

Las radiografías del tórax exponen una masa redonda densa localizada mayormente en el lóbulo inferior derecho, siguiéndole en frecuencia el lóbulo inferior izquierdo y luego, el lóbulo superior izquierdo según Hepburn (5) o el lóbulo medio derecho según Faifbairn (4). La masa puede verse pulsar en fluroscopía del área de la fístula. Con este procedimiento, ésta puede disminuir de tamaño al ejecutar la maniobra de Valsalva y agrandarse con la maniobra de Mueller. Las laminografías del área demostrarán vasos aferentes y eferentes a la masa. El diagnóstico se confirma con la angiografía pulmonar. El electrocardiograma es normal en la mayoría de los casos.

Las fístulas arteriovenosas pulmonares se asocian a otras anomalías vasculares, como telangiectasis de las mucosas (síndrome de Rendu-Osler-Weber) y a otras fístulas arteriovenosas en otras partes del cuerpo como el sistema gastrointestinal, la vejiga urinaria, etc. (7).

Las complicaciones que más frecuentemente se asocian a esta anomalía son: la rotura de la fístula, la que produce hematoma en el pulmón o hemotórax, hipertensión pulmonar, policitemia, accidentes cerebro vasculares y abscesos cerebrales.

El tratamiento de esta anomalía es la corrección quirúrgica de la misma, ya que revierte la hipoxemia, se corrige el cortocircuito de sangre, y se evitan las complicaciones que hemos mencionado. Fairbairn, (4) basado en la experiencia de la Clínica Mayo, recomienda cirugía en la mayoría de los casos excepto en pacientes con una sola fístula que estén asintomáticos, que no tengan el síndrome de Rendu-Osler-Weber. Estos pacientes se operarían solo si la fístula crece de tamaño, o si desarrollaran síntomas.

Resumen

Este es el caso de un joven de 18 años que presentaba una fístula arteriovenosa pulmonar en el hilio izquierdo. Esta se desarrolló años después de que el paciente fuera sometido a una intervención quirúr-

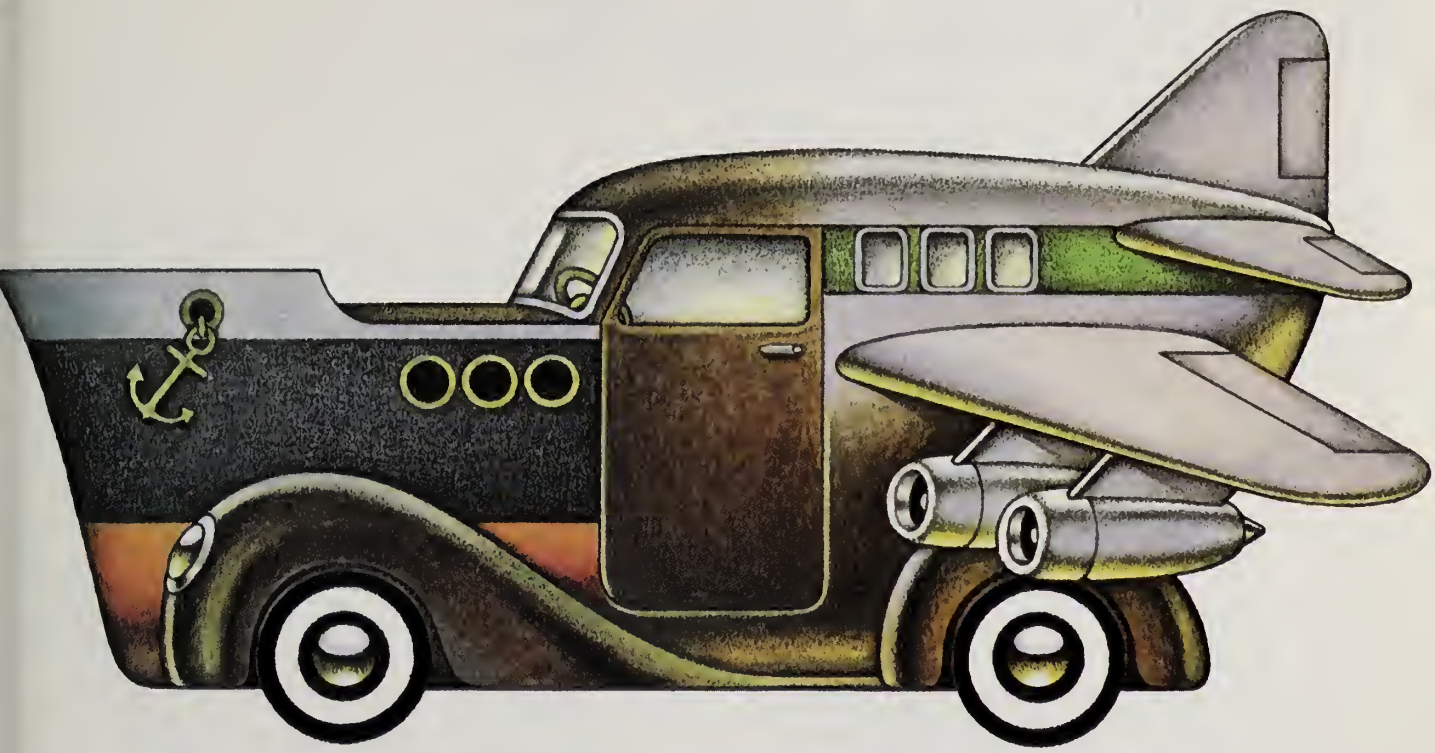
gica por una lesión similar en el lóbulo inferior del pulmón derecho. La lesión era de tipo congénito y no se intentó remover la anomalía debido a la posición y tamaño de la misma. Los estudios radiográficos, como ilustrativos de esta condición, confirmaron el diagnóstico. Llegamos a la conclusión que el tratamiento quirúrgico debe ser ejecutado temprano en aquellos casos que el abordamiento a la lesión lo permita, ya que este proceder es eficaz en la mayoría de los casos.

Summary

This paper presents the case of a 18 year old male patient with a congenital pulmonary arteriovenous fistula which was diagnosed after having had a right inferior lobectomy for a similar anomaly several years prior to the present diagnosis. The radiographic studies done are presented as an illustration of the anomaly, and the literature was reviewed. We conclude that the pulmonary arteriovenous fistulas should be surgically removed when feasible since this could mean total cure in the majority of the patients.

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Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

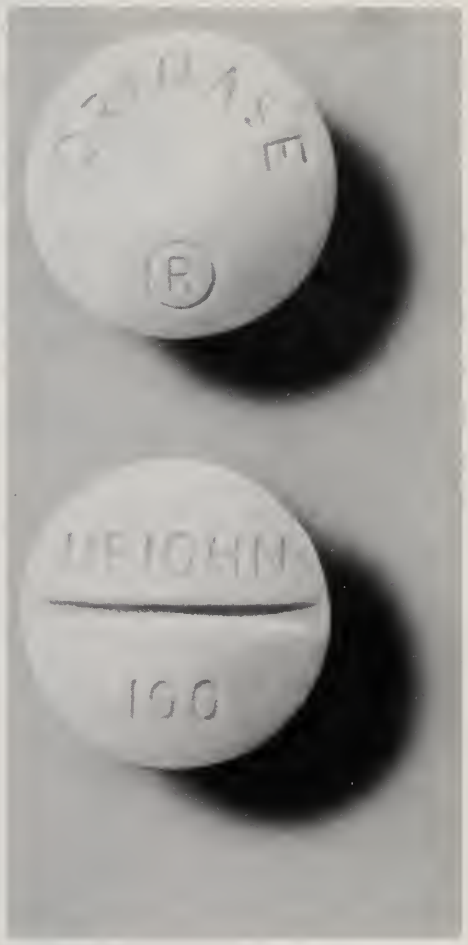
Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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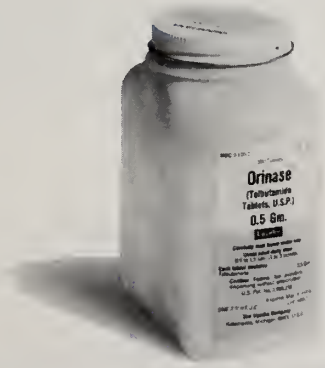
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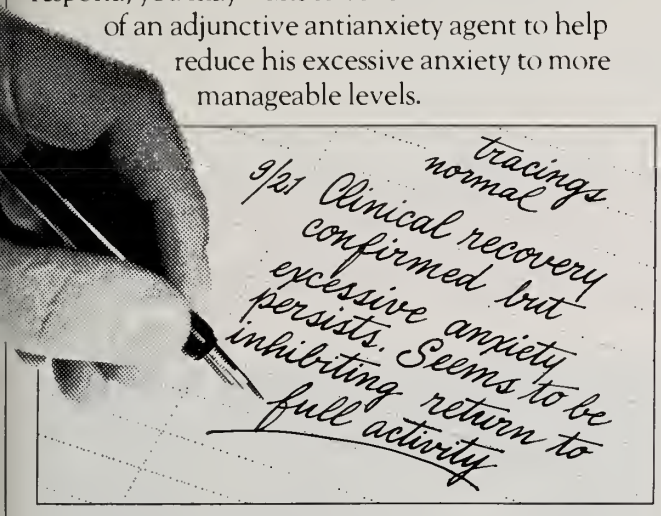
Clinical anxiety, for example, may be one reason for prolonged recuperation following cardiac healing. Yet anxiety can sometimes be beneficial in facilitating patient compliance.

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patient's ability to participate fully in his rehabilitation program, your counseling and reassurance are often sufficient. But when his anxiety is so great that it actually interferes with his ability to listen and respond, you may want to consider the addition of an adjunctive antianxiety agent to help reduce his excessive anxiety to more manageable levels.



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Performance: Hundreds of clinical trials, thousands of published papers, and millions of patients comprise the record of performance for Librium.

Concomitant use: Of special significance in treating the cardiac patient already taking multiple agents is the fact that Librium is used concomitantly with most primary medications, such as cardiac glycosides, diuretics and antihypertensives.

*Zohman BL: *Geriatrics* 28.110-119, Feb 1973

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Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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Contraindications: Children 14 years of age and under; pregnant women and nursing mothers; active gastrointestinal lesions or history of recurrent gastrointestinal lesions; allergy to aspirin or indomethacin.

Warnings: *Gastrointestinal Effects:* Because of the occurrence and, at times, severity of gastrointestinal reactions, be continuously alert for any sign or symptom signaling a possible gastrointestinal reaction. The risks of continuing therapy with INDOCIN in the face of such symptoms must be weighed against the possible benefits to the individual patient. Gastrointestinal effects may be reduced by giving the drug immediately after meals, with food, or with antacids. Use greater care in aging patients.

Ocular Effects: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients on prolonged therapy. Discontinue therapy if such changes are observed. Ophthalmologic examination at periodic intervals is desirable in patients on prolonged therapy.

Central Nervous System Effects: INDOCIN may aggravate psychiatric disturbances, epilepsy, and parkinsonism, and should be used with considerable caution in patients with these conditions. If severe CNS adverse reactions develop, discontinue the drug.

Precautions: Blurred vision may be a significant symptom that warrants a thorough ophthalmologic examination. Patients should be cautioned about engaging in activities requiring mental alertness and motor coordination, as driving a car. Headache which persists despite dosage reduction requires complete cessation of the drug. May mask the usual signs and symptoms of infection; therefore, the physician must be continually on the alert for this and should use the drug with extra care in the presence of existing controlled infection. After the acute phase of the disease is under control, an attempt to reduce the daily dose should be made repeatedly until the patient is off entirely.

Drug Interactions: Although INDOCIN has not influenced the hypoprothrombinemia produced by anticoagulants, patients on anticoagulant therapy should be observed closely for alterations in prothrombin time. In patients receiving probenecid, plasma levels of indomethacin are likely to be increased and a lower total daily dose of INDOCIN may produce a therapeutic effect; increases in the dose of INDOCIN should be made cautiously and in small increments.

Adverse Reactions: *Gastrointestinal Reactions:* Single or multiple ulcerations of the esophagus, stomach, duodenum, or small intestine, including perforation and hemorrhage, with fatalities in some instances; rarely, intestinal ulceration has been associated with stenosis and obstruction; gastrointestinal bleeding without obvious ulcer formation; perforation of preexisting sigmoid lesions (diverticulum, carcinoma, etc.); rarely, increased abdominal pain in ulcerative colitis patients or development of ulcerative colitis and regional ileitis; gastritis may persist after the cessation of the drug; nausea, vomiting, anorexia, epigastric distress, abdominal pain, and diarrhea.

Eye Reactions: Corneal deposits and retinal disturbances, including those of the macula, have been observed on prolonged therapy; blurring of vision.

Hepatic Reactions: Rarely, toxic hepatitis and jaundice, including some fatal cases.

Hematologic Reactions: Aplastic anemia, hemolytic anemia, bone marrow depression, agranulocytosis, leukopenia, and thrombocytopenic purpura may occur rarely. Since some patients manifest anemia secondary to obvious or occult gastrointestinal bleeding, appropriate blood determinations are recommended.

Hypersensitivity Reactions: Acute respiratory distress, a rapid fall in blood pressure resembling a shock-like state, angioedema, dyspnea, asthma, angiitis, pruritus, urticaria, skin rashes, purpura.

Ear Reactions: Hearing disturbances—deafness reported rarely; tinnitus.

Central Nervous System Reactions: Psychic disturbances including psychotic episodes, depersonalization, depression, and mental confusion; coma; convulsions; peripheral neuropathy; drowsiness; lightheadedness; dizziness; syncope; headache.

Cardiovascular-Renal Reactions: Edema, elevation of blood pressure, hematuria.

Dermatologic Reactions: Loss of hair, erythema nodosum.

Miscellaneous: Rarely, vaginal bleeding, hyperglycemia, glycosuria, ulcerative stomatitis, and epistaxis.

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TIROIDITIS CRONICA LINFOCITARIA ASOCIADA AL SINDROME DE SARAMPION ALEMAN CONGENITO: Informe de un Caso

A. Pérez Comas, MD, PhD

La asociación del síndrome de sarampión alemán congénito con tiroiditis crónica linfocitaria o con hipotiroidismo adquirido no ha sido informada previamente. La asociación de endocrinopatías con el síndrome del sarampión alemán congénito tan solo había sido sugerida en diabetes mellitus por Forrest y Menser (1) en 1971 y con hipertiroidismo por Ziring y colaboradores (2) en 1975.

En los últimos dos años y medio hemos seguido en nuestro consultorio una niña afecta de sordomudez congénita secundaria al síndrome del sarampión alemán congénito, quien además presenta hipotiroidismo adquirido secundario a tiroiditis crónica linfocitaria.

Presentación del Caso

W. B. nació a término de una madre de 23 años de edad, y un padre no consanguíneo de 25 años de edad, tras una gestación complicada por sarampión alemán en la madre a la quinta semana del embarazo. Presentó un peso al nacer de 7 libras, un largo de 20 pulgadas, y no observaron anormalidad alguna al nacer. Su desarrollo psicomotor fue aparentemente normal, excepto por sordera confirmada a los 9 meses de edad. Fue evaluada en un hospital de Nueva York donde le proveyeron audífonos especiales.

La niña estuvo relativamente bien, salvo por su defecto con la audición y los problemas secundarios del habla, hasta aproximadamente los 3 años de edad, cuando su madre comenzó a notarle estreñimiento, disminución del apetito, palidez, somnolencia frecuente y crecimiento lento. Al estudiar sus gráficas de percentila en estatura y peso (Figura 1), observamos que el enlentecimiento en su crecimiento longitudinal comienza alrededor de los 28 meses de edad.

A la edad de cuatro años y diez meses de edad nos fue referida y el diagnóstico de hipotiroidismo adquirido fue hecho (Figura 2). Presentaba un peso de 36 libras, una estatura de 37 pulgadas, un segmento inferior de 20 pulgadas, un segmento superior de 17 pulgadas, un S.S./S.I. de 1.18, facies con rasgos asperos, piel reseca y fría, ligero estrabismo convergente, tiroides agrandada IX sobre el tamaño normal, firme, blanda y bien delimitada, bradicardia (64/min), normotensión (85/60) y normorrefléxica. Presentaba también sordera marcada. El estudio dermatoglífico reveló ángulos atd normales, surcos de flexión en las palmas normales, pero con abundantes líneas en las palmas.

La edad ósea combinada (codo-muñeca-pelvis-rodilla-pié) fue compatible con 3 años de edad. El nivel de T-4 total fue de 0.10 (normal 3.1-7.0) ugT4l por ciento, la captación en resina de T-3 35.9 (N = 41-55), el PBI 1.5 ug por ciento (N = 4-8), el índice de tiroxina libre menor de 0.26 (N = 2.6 -8.0), el colesterol sérico mayor de 500 mg por ciento. Las radiografías de pecho y lateral de cráneo fueron informadas como normales. Los anticuerpos de tiroides por hemaglutina-

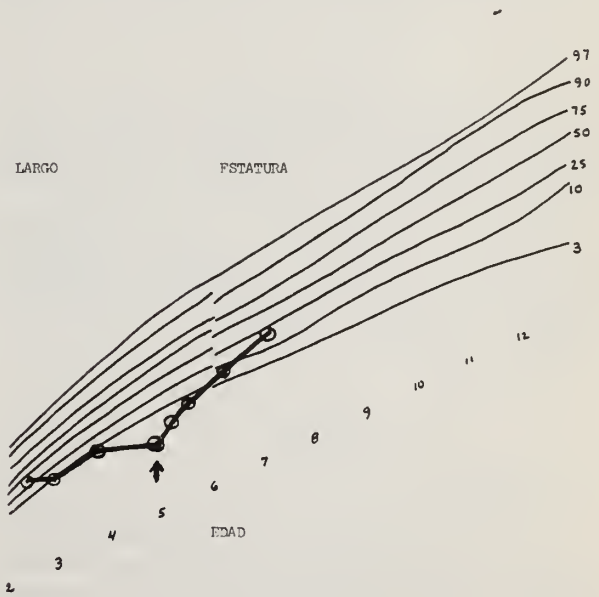


Figura 1: *Tabla de percentila de estatura. La flecha indica comienzo de tratamiento.*

De la Sección de Endocrinología Pediátrica y Genética Médica, Hospital Dr. Ramón E. Betances, Centro Médico de Mayagüez.



Figura 2: *Paciente a los 4 años, 10 meses de edad.*

ción fueron positivos hasta una dilución de 1/250. La captación de radioiodo fue 5.7 por ciento a las 2 hras., 6.6 por ciento a las 4 horas y 3.2 por ciento a las 24 horas (normal 10-35 por ciento).

Inicialmente recibió Euthroid-1 y luego a los 6 años requirió que se le incrementara la dosis a una y media tableta al día de Euthroid-1. A los 7 años pesa 47 libras, mide 45 1/2 pulgadas y está asistiendo a un grupo especial donde presenta un nivel de aprendizaje excelente.

Discusión

El síndrome de sarampión alemán congénito es secundario a la infección de la madre por sarampión alemán durante el embarazo, mayormente en los primeros 3 meses de embarazo (3). Los defectos permanentes más comunes son cataratas, anomalías cardíacas, especialmente ducto arterioso, sordera y mudez secundaria, microcefalia y retardación mental. Condiciones menos frecuentes son microftalmia, buftalmos, lesiones retinianas, "talipes equinovarus", sindactilia, hipospadias, debilidad muscular generalizada, diplegía cerebral, paladar hendido y anomalías dentales (4).

El grado de afectación del recién nacido es variable, depende de la intensidad de la infección en el niño y el período cuando ésta le afectó durante el embarazo. La mayor incidencia de lesiones, y cuando más severas son, ocurre en el primer trimestre del embarazo, durante el período de organogénesis. Cuando la infección ha sido severa, el bajo peso al nacer es uno de los hallazgos más frecuentes al nacer. Durante los primeros días de vida la infección puede recrudecerse y el infante vivir los primeros 6 meses de vida con problemas serios, tales como trombocitopenia, anemia, hepatitis, pneumonitis, encefalitis, rinitis, otitis media, fallo cardíaco congestivo y diarrea. En ocasiones las complicaciones neurológicas no se observan o se definen hasta transcurrido el año de edad. El virus puede ser cultivado de las capas internas del lente hasta 3 años después de nacido.

Forrest y Menser (1), en 1971 encontraron una mayor incidencia de sujetos afectos de diabetes mellitus en jóvenes adultos con el síndrome de sarampión alemán congénito, comparado con la población no afectada. Recientemente Ziring y colaboradores (2), encuentran una niña afecta de hipertiroidismo y este síndrome, surgiendo una posible relación entre endocrinopatías y el síndrome de sarampión alemán congénito.

Nuestra paciente presenta el síndrome de sordera congénita e hipotiroidismo adquirido, secundario a tiroiditis crónica de Hashimoto. Previo a nuestra paciente, esta condición no había sido informada asociada con el síndrome de sarampión alemán congénito (3).

La causa de la diabetes mellitus, el hipertiroidismo y la tiroiditis crónica linfocitaria es desconocida. Se sospecha que en algunos casos de diabetes mellitus existe un factor autoinmune, debido a que con frecuencia y en ciertos grupos de pacientes, se asocia con tiroiditis de Hashimoto y otras condiciones donde se sospecha exista una etiología autoinmune. En el hipertiroidismo también se menciona un posible factor autoinmune. Nosotros hemos observado, por ejemplo, que casi un 20 por ciento de nuestros pacientes diabéticos juveniles presentan patología tiroidea, encontrándose un por ciento elevado de éstos con anticuerpos a tiroides positivos (6). Estos datos preliminares tienden a confirmar que tenemos un grupo de diabéticos con posible factor o factores autoinmunes.

Por nuestros hallazgos, por los de Forrest y Menser

(1) y los de Ziring y colaboradores (2), sospechamos que en el síndrome del sarampión alemán congénito cabe la posibilidad de que se produzcan trastornos inmunológicos secundarios a la infección por el virus, y que en estos casos de lugar a diversos tipos de endocrinopatías según el órgano que se afecte.

El estudio de función tiroidea, de los niveles de anticuerpos a tiroides y de anticuerpos a otros órganos del cuerpo, podría ayudar a establecer estos mecanismos en los sujetos afectos del síndrome de sarampión alemán congénito.

Nuestra paciente solo presenta como estigma del síndrome de sarampión alemán congénito la sordera, el mutismo secundario a la sordera, y el exceso de líneas palmares en análisis dermatoglífico. Resalta el hecho de que en su tabla de percentilas el crecimiento se retardó antes de que comenzaran los síntomas clínicos de forma marcada, observándose una disminución en la percentila. Esto vuelve a recalcar, una vez más, la utilidad extrema para el pediatra de estas tablas comparativas. No solo basta el hecho de pesar y medir a distintas edades, sino que hay que establecer el patrón de crecimiento normal del niño. Tan solo de esta forma sabremos si hay alguna desviación anormal.

Los niveles elevados de anticuerpos a tiroides por hemaglutinación confirman la presencia, en esta paciente, de una enfermedad autoinmune tiroidea como es la tiroiditis crónica de Hashimoto. El realizar una biopsia abierta de tiroides sería académico y conllevaría una cicatriz. Se descarta el síndrome de Pendred que incluye bocio - sordera y trastornos de captación y descarga de radioiodo, y que es autosómica recesiva, ya que la niña no presentó bocio, ni hipotiroidismo durante los primeros tres años, no se observa una captación elevada de radioiodo en las primeras horas con descarga aumentada (como se vería en el síndrome de Pendred) y los anticuerpos a tiroides positivos nos confirman tiroiditis crónica de Hashimoto.

Resumen

La asociación del síndrome de sarampión alemán y tiroiditis crónica de Hashimoto no había sido informada previamente. Esta comunicación informa de una niña donde se presentan ambas condiciones. El hecho de que se hayan informado casos de hipertiroidismo, tiroiditis crónica y de diabetes mellitus en pacientes con el síndrome de sarampión alemán congénito, hace pensar en algún trastorno inmunológico secundario a la lesión producida por el virus en diversos órganos.

Summary

This paper reports the coexistence of congenital rubella syndrome and acquired hypothyroidism secondary to Hashimoto's thyroiditis in a Puerto Rican female child. Due to previous reports of increased incidence of diabetes mellitus among patients with the congenital rubella syndrome, to a recent report of thyrotoxicosis associated with the syndrome, and to our patient, the possibility of immunologic derangement secondary to rubella virus lesion to different organs is presented. Studies of different tissues autoantibodies should be helpful in elucidating this interesting hypothesis in patients with the congenital rubella syndrome.

Reconocimiento

Agradecemos a la Dra. Esther Ramírez de Falletti el habernos referido esta paciente a nuestro consultorio, al Departamento de Fotografía del Centro Médico de Mayagüez por las preparaciones fotográficas y a la Sra. Mirna Nazario por la excelente labor secretarial.

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SPECIAL COMMUNICATION: DIAGNOSTIC PATTERNS IN DISABILITY IN PUERTO RICO AND THE UNITED STATES

Jaime F. Pou, MD

This short statistical analysis of data compiled by the Office of Research and Statistics, Social Security Administration, shows the extent and nature of Puerto Rico's participation in the social security disability insurance program. It compares some of the Commonwealth's data with national averages, and includes a comparison of worker disability allowances by diagnostic groups for Puerto Rico and the United States of America overall.

Under the provisions of the social security disability program, the nation's largest disability plan, a worker under 65 can receive monthly benefits if he or she becomes unable to work due to a mental or physical impairment that has lasted—or is expected to last—at least 12 months or is expected to result in death.

Almost 80 million workers can count on monthly cash benefits in the event of such severe and extended disability. In addition, the dependents of these workers are also eligible for monthly benefits. Nearly 2.4 (1970-1.8m) million workers and 1.8 (1970-1.4m) million dependents are now receiving disability benefits at the rate of more than $7.5 (1970-$5 billion) billion a year.

Currently, 51,000 (1970-31,368) disabled workers in Puerto Rico are receiving $8,500,000 (1970-4,092,423) a month in benefits. In addition, 17,000 (1970-11,275) wives or husbands of disabled workers and 69,000 (1970-45,468) children of disabled workers in Puerto Rico are receiving benefits at a monthly rate of $590,000 (1970-$304,627) and $2,070,000 (1970-$1,017,709), respectively. The latest year for which tabulated data is available showing disabled worker diagnostic patterns by State is 1972. Disabled workers in Puerto Rico who began receiving benefits in that year constituted 6431 (1970-5,096) of the 455,398 (1970-350,384) new beneficiaries nationwide.

Table I compares the frequency of diagnostic groups in Puerto Rico with the U. S. overall. It shows that diseases of the circulatory system comprised the largest diagnostic group in the country in 1972. Diseases of the musculoskeletal system and mental disorders, including psychoneurotic and personality disorders, were the second and third largest diagnostic groups, respectively. All States do not, however, follow this pattern.

Within these overall diagnostic groups, the most prevalent *primary diagnosis* in the nation in 1972 was chronic ischemic heart disease. Puerto Rico recorded 579 (1970-474) cases that year. The nation's second most common primary diagnosis, osteoarthritis, accounted for 227 (1970-204) cases in Puerto Rico. Following these, in order of decreasing national prevalence, was displacement of intervertebral disc, with Puerto Rico reporting 260 (1970-215) cases, followed by schizophrenia with 1,296 (1970-

Medical Consultant, Disability Determination Program, Social Security Administration.

TABLE I
SOCIAL SECURITY WORKER DISABILITY ALLOWANCES 1972
DIAGNOSTIC GROUPS

Diagnostic Group	1972 U. S.		1972 Puerto Rico		1970
Diseases of the circulatory system	146,684	32.2 °/o	1,024	15.9 °/o	17.3 °/o
Diseases of the musculoskeletal system	75,923	16.7 °/o	971	15.1 °/o	13.7 °/o
Mental, psychoneurotic, and personality disorders	45,253	9.9 °/o	2,202	34.2 °/o	34.1 °/o
Neoplasms	43,667	9.6 °/o	336	5.2 °/o	5.8 °/o
Accidents, poisonings, and violence	31,728	7.0 °/o	311	4.8 °/o	6.7 °/o
Diseases of the respiratory system	33,038	7.3 °/o	306	4.8 °/o	3.9 °/o
Diseases of the nervous system and sense organs	28,216	6.2 °/o	561	8.7 °/o	7.2 °/o
Endocrine system, metabolic, and nutritional diseases	17,352	3.8 °/o	261	4.1 °/o	3.6 °/o
Diseases of the digestive system	13,369	2.9 °/o	186	2.9 °/o	2.2 °/o
Infective and parasitic diseases	8,627	1.9 °/o	127	2.0 °/o	2.2 °/o
Other	11,541	2.5 °/o	146	2.3 °/o	3.1 °/o
TOTAL -	455,398	100.0 (1)	6,431	100.0 (1)	

(1) - *Figures may not total 100 °/o due to rounding.*

1,007) cases. There were 122 (1970-79) cases of emphysema in Puerto Rico; 179 (1970-147) cases of diabetes mellitus, and rheumatoid arthritis and allied conditions accounted for 76 (1970-37) cases in Puerto Rico that year. Acute cerebrovascular disease, listed eighth among the most prevalent primary diagnoses in 1972, recorded 66 (1970-68) cases in Puerto Rico; malignant neoplasm of trachea and lung 9 (1970-22) cases; and other respiratory diseases ranked tenth with 26 cases.

A similar comparative statistical study of disabilities was made in 1970. The result of that study was reported in Boletín de la Asociación Médica de Puerto Rico in November 1973.

NOTICIAS

ANNOUNCEMENT FROM THE U. S. VIRGIN ISLANDS MEDICAL SOCIETY

The second Mid-Winter Virgin Islands Clinical Conference will be held in St. Croix, January 13, 14, 15, 1977 by the U. S. Virgin Islands Medical Society in association with The Faculty of the University of Pennsylvania School of Medicine.

This program is acceptable for 14 credit hours in Category 1 for the Physician's Recognition Award of the A. M. A., and will include lectures and seminars of interest to the physician in General Practice, Internal Medicine, General Surgery, OB-Gyn and Pediatrics.

For further information, write AIRMAIL to:

James S. Glenn, M. D., F.A.C.P.
Chaim Chairman
U. S. Virgin Islands Medical Society
P. O. Box 520
Christiansted, St. Croix
U. S. Virgin Islands 00820

January 24-28, 1977. 4TH ANNUAL POSTGRADUATE COURSE IN MODERN PRACTICAL NEUROLOGY. Miami Beach, Florida. Sponsored by the Department of Neurology, University of Miami School of Medicine. AMA Accredited, Category 1 26 hrs. minimum, 32 hrs. maximum. Information: Division of Continuing Medical Education, University of Miami School of Medicine, P. O. Box 520875, Miami, Fla. 33152: (305) 547-6716.

The Second Annual Mid-American Breast Cancer Symposium will be held November 5-6 in Madison, Wisconsin's Concourse Hotel.

Convened in honor of Robert Egan, M. D., a pioneer in the field of mammography, the symposium will feature sixteen distinguished faculty members from the United States, Canada and the Netherlands.

They include N. J. M. Aaarts, M. D., president of the European Thermography Society, Tilburg, Netherlands; M. W. Asplund, M. D., director of the community breast screening program, Bloomer, WI; Richard Byrne, M. D., department of radiology, Columbia Hospital, Milwaukee, WI; Donald E. Bauermeister, M. D., chief of pathology, Virginia Mason Medical Center, Seattle, WA;

John R. Cameron, Ph.D., professor of radiology and physics, University of Wisconsin, Madison, WI; George Crile, Jr., M. D., surgeon, Cleveland Clinic, Cleveland, OH; Robert Egan, M. D., chief section of mammography, Emory University School of Medicine, Atlanta, GA; Larmon A. Gray, M. D., clinical professor of OB-GYN, University of Louisville, Louisville, KY:

Robert Hutter, M. D., director of the department of pathology, St. Barnabas Medical Center, Livingston, N. J., Harold Isard, M. D., chairman, division of pathology, Albert Einstein Medical Center, Philadelphia, PA; Lester Kalisher, M. D., head radiologist, mammography soft tissue section, Massachusetts General Hospital, Boston, MA; Ray Lawson, M. D., surgeon, McGill University, Westmount Breast Cancer, Montreal, Quebec;

William Melton, American College of Radiology, Chevy Chase, MD; Anthony Miller, F.R.C.P., director, epidemiology unit, National Cancer Institute of Canada, Toronto, Ontario; Myron Moskowitz, M. D., associate professor of radiology, project director, Breast Cancer Detection Center, Cincinnati, OH; and Philip Strax, M. D., medical director, Guttman Institute, New York City, NY.

Enrollment for the symposium, which meets the criteria for 12 hours of credit in category 2 for the Physician's Recognition Award of the American Medical Association, is limited to 300. Registration fee is $75, $35 for interns or residents.

For additional information, write: William B. Hobbins, president, Wisconsin Breast Cancer Detection Foundation, Inc., 7803 Mineral Point Road, Madison, WI 53717.

HEW NEWS:

A revised schedule of limits on coverage of hospital costs under Medicare was announced today by the Department of Health, Education, and Welfare.

The new schedule, published in today's Federal Register, applies to hospital cost report periods beginning on or after July 1, 1976, replacing the schedule now in effect. The new limits generally reflect increases in hospital costs over the past year.

The limitations are authorized by law and establish ceilings beyond which costs are deemed to be in excess of those necessary to provide efficiently delivered health services. The schedule of limits takes into account differences in hospital size and geographical location in arriving at a ceiling that can be applied to individual hospitals.

The new limits will enable HEW more effectively to identify hospitals whose costs are substantially higher than those necessary for efficient delivery of hospital inpatient services.

The Department of Health, Education, and Welfare today proposed regulations to provide a uniform period of 60 days during which a person claiming benefits can request reconsideration of an adverse decision.

The regulations apply to retirement, survivors, disability, black lung, hospital insurance, and supplemental security income programs administered by the Social Security Administration. They provide the same time period for requesting reconsideration as provided by Public Law 94-202, enacted January 2, 1976, which established a period of 60 days during which a hearing could be requested.

The proposed regulations reduce from 6 months to 60 days the time allowed to request a reconsideration on social security, Medicare, and black lung determinations, and increase the SSI time period from 30 to 60 days.

To protect claimants in cases where a time limit has expired, SSA has procedures under which an initial determination may be reopened. In addition, SSA regulations provide for an extension of the time allowed to file for a reconsideration if good cause is established for not filing on time.

Interested parties have 45 days after today's publication of the proposed regulations in the Federal Register to submit comments.

The Department of Health, Education, and Welfare today published final regulations under which the Social Security Administration will no longer disclose the location of an absent parent to courts and State welfare agencies, but will, instead, make such disclosures to the Federal Parent Locator Service to enforce child-support obligations.

Until a change in the law became effective August 1, 1975, SSA had released the address of an absent parent or that of his last employer directly to courts and State welfare agencies on request for the purpose of enforcing support obligations. Under the new law, the name and most recent address of an absent parent, his social security number, and the address of his last employer will be disclosed only to the Federal Parent Locator Service, which may transmit such information to States and other authorized persons under Title IV, Part D of the Social Security Act.

The regulations take effect with today's publication in the Federal Register.

POSTGRADUATE COURSE ON INFECTIOUS DISEASES SET FOR BALTIMORE

Philadelphia, PA. – The American College of Physicians (ACP) will sponsor a three-day postgraduate course on infectious diseases Sept. 15-17, 1976, Baltimore, Md. The course will be co-sponsored by the University of Maryland School of Medicine.

For information and registration: Registrar, Postgraduate Courses, ACP, 4200 Pine Street, Philadelphia, Pa. 19104.

AMA NEWS RELEASES:

PROGRESS REPORTED IN COPING WITH DISABLED PHYSICIANS:

Chicago – The American Medical Association this month reports substantial progress in its program to cope with disabled physicians.

Indications are that some 20 state medical societies have now initiated, or are in the process of formulating, programs to identify, treat and rehabilitate physicians who are mentally ill or who are suffering from alcoholism or drug dependence, the AMA said.

Several states, including Utah, New Mexico, Nebraska and Kansas, have enacted disabled physician legislation in 1976 that includes the principal aspects of the AMA model bill on impaired physicians.

The AMA House of Delegates last winter asked all state medical societies "to urge adoption of the AMA model bill known as the 'Disabled Physicians Act' by the legislatures of their respective jurisdictions."

State society program representatives from Michigan, Maryland, Florida, Ohio and Illinois met last winter to discuss implementation of the program. They agreed that the program should include a campaign of publicity and promotion, including distribution of printed material to every physician in the state.

This spring program representatives from Arizona, California, Oregon, Utah and Washington held a similar conference. They urged encouragement of a good relationship between the medical society and the state licensing board, with formal mechanisms for communications, and stressed that physicians should be reached *before* they become a danger to themselves and their patients. Valid referrals should be encouraged from colleagues, spouses, office personnel, hospital staffs, answering services, narcotics agents and medical society executives.

The AMA's model state legislation begins: "An Act Concerning the Practice of Medicine. To provide for the restriction, suspension or revocation of the license of any physician to

practice medicine because of his inability to practice medicine with reasonable skill and safety to patients, due to physical or mental illness, including deterioration through the aging process or loss of motor skill, or abuse of drugs, including alcohol."

AMA ETHICS PERMIT PHYSICIAN ADVERTISING

Chicago – The Principles of Medical Ethics of the American Medical Association do *not* prohibit advertising by physicians, declares a statement in the May 24 issue of the Journal of the American Medical Association.

In reaffirming the long-standing AMA policy on advertising by medical doctors, the AMA's Judicial Council pointed out that the prescription is not against advertising, but concerns soliciting of patients.

The public is entitled to know the names of physicians, the type of their practices, the location of their offices, their office hours, and "other useful information that will enable people to make a more informed choice of physician," the AMA Council points out.

"The physician may furnish this information through the accepted local media of advertising or communication, which are open to all physicians on like conditions. Office signs, professional cards, dignified announcements, telephone directory listings, and reputable directories are examples of acceptable media for making information available to the public."

A physician may give biographical and other relevant data for listing in a reputable directory. The published data may include the charge for a standard office visit, or the doctor's fee or range of fees for specific types of services.

The statement points out that local, state or medical specialty associations are autonomous, and may have ethical restrictions that exceed the Principles of Medical Ethics. And, legal restrictions on advertising or solicitation of patients exist in the medical licensure laws of at least 34 states.

In the proscribed area of solicitation of patients, the Council points out that it is unethical to use testimonials, create inflated or unjustified expectations of favorable results, make statements that are self-laudatory and imply that the physician has skills superior to others, or use incorrect or incomplete facts that are likely to cause the average person to misunderstand or be deceived.

"Physicians have an ethical duty to subordinate financial reward to social responsibility. A physician should not engage in practices for pecuniary gain that interfere with his medical judgment and skill or cause a deterioration of the quality of medical care. Ability to pay should be considered in reducing fees, and excessive fees are unethical.

"Physicians should not pay commissions or rebates or give kickbacks for the referral of patients. Likewise, they should not make extravagant claims or proclaim extraordinary skills. Such practices, however common they may be in the commercial world, are unethical in the practice of medicine because they are injurious to the public."

The statement is signed by Henry I. Fineberg, M. D., of New York, AMA Judicial Council chairman, and the four other members.

PATIENTS FAIL TO KEEP UP TREATMENT FOR HIGH BLOOD PRESSURE

Chicago – Health is, to a large degree, a matter of personal responsibility, declares an editorial in the May 24 issue of the Journal of the American Medical Association.

Many people believe that health care is synonymous with medical care, but, as a general rule, medical care has relatively little impact on health, says William R. Barclay, M. D., JAMA editor.

Measurements that supposedly reflect health, such as illness, longevity, growth, and development, are not measures of quality of medical care being received, Dr. Barclay points out.

There is a notable exception to this premise, however – high blood pressure. Medical care can detect and treat high blood pressure, thus reducing a primary cause of ill health and death for many Americans, he says.

Progress has been made in informing the public and the health professionals that high blood pressure is a serious problem meriting serious attention. And progress has been made in creating a system of mass screening of the population.

But there still is much to be done in developing follow-up and effective treatment programs, Dr. Barclay declares.

"Effective drugs are available, and physicians are knowledgeable in their use, but the problem of patient compliance is unsolved. Most people are reluctant to take a daily medication over a period of years, or possibly for the rest of their lives, especially if they have no symptoms."

Perhaps the social and behavioral sciences need to be brought into play more extensively, and the solution may lie not with health professionals but in the expertise of other professional groups, he says.

In the same issue of JAMA, Jeremiah Stamler, M. D., of Northwestern University Medical School in Chicago, and colleagues reports on results of the screening of more than one million persons in the nationwide Community Hypertension Evaluation Clinic (CHEC) program.

CHEC confirmed the scope of the problem in the United States, with the finding that of those screened 247 of 1,000 had elevated blood pressure. The survey also confirmed that much high blood pressure is untreated. More than half of those with elevated pressure were not being treated effectively, Dr. Stamler says.

High blood pressure is also a problem in children, says Patricia T. Pazdral and colleageus in another JAMA article, urging pediatricians and other physicians treating children to take blood pressure readings.

in Brief
A summary of AMA, medical & health news
American Medical Association / 535 North Dearborn Street / Chicago, Illinois 60610 / Phone (312) 751-6000 / TWX 910-221-0300

HEW's new proposed Utilization Review Regulations show "beneficial changes" from earlier regulations published in November of 1974, the AMA said, but the Association urged the deletion from the regulations of the requirement that elective surgical or other elective procedures under Medicare and Medicaid be delayed until hospital admission had been determined medically necessary. The AMA stated that the requirement could apply to almost every procedure and could delay the treatment of patients and that "any delay prior to proceeding with the surgery or procedure will increase the hospitalization cost." Among the beneficial changes, the AMA said, are the authorization of medical staffs to develop their own criteria for reviewing hospital admissions, and the right of the medical staff to establish a list of diagnoses, conditions, or procedures which would need no further justification for admission.

AMACO--American Medical Assurance Company --the AMA's reinsurance company will provide reinsurance backing and technical support to qualifying physician-owned medical liability companies in the near future. Representatives of state medical societies met in Chicago last month and heard discussion from AMA staff, reinsurance and insurance officials on the subject. Fifteen physician-owned companies are now in operation or will be in a few months.

The AMA asked the FTC to "clarify its clarification" of a statement submitted in the Federal Trade Commission's antitrust complaint against the AMA, the Connecticut State Medical Society and the New Haven County Medical Assn. In the statement the FTC said its complaint charges the AMA "with a great deal more than merely imposing 'certain restrictions on advertising' " by physicians. It said the "entire panoply of restrictive agreements contained in the *Principles of Medical Ethics* is under attack." The AMA said the FTC complaint violates due process provisions of the Administrative Procedure Act and is so "nebulous" that a defense cannot be prepared. The antitrust complaint is scheduled to be heard Oct. 18 before an FTC administrative law judge.

The AMA is aiding the medical staff of St. John's Regional Medical Center in a lawsuit before the South Dakota Supreme Court. The hospital is appealing a circuit court decision invalidating changes in the medical staff bylaws on the grounds that they were unilaterally amended by the hospital's board of directors without the approval of the medical staff. At the request of the South Dakota State Medical Assn., the AMA began helping the medical staff while the case was before the circuit court.

The AMA will participate in HEW's new "fraud and abuse initiative" program to crack down on the "dishonest activities of some Medicaid providers and clear the image of the overwhelming majority who are honest." C. Willard Camalier Jr., MD, chairman of the AMA's Council on Medical Services, who was a speaker at the meeting, said the AMA was enthusiastic about the HEW effort because "we too are convinced that a very small minority of Medicaid providers are actually engaged in fraudulent or abusive practices." Dr. Camalier added that the AMA's newly established Ad Hoc Committee on Medical Discipline could offer suggestions on methods of dealing with the problem.

The AMA asked to join as a co-plaintiff the state of North Carolina's lawsuit against the federal government's National Health Planning and Resources Development Act. The AMA charges that the planning law, passed in 1974 and now being implemented, violates at least five amendments to the Constitution.

A successful countersuit by an Illinois physician against a patient and the attorneys who had charged him with malpractice was termed "significant" by AMA President Max H. Parrott, MD, "because it serves notice that doctors intend to fight back against non-meritorious cases and puts lawyers on notice that they are placing themselves in jeopardy if they do not adequately investigate a case before filing it." If the case stands up on appeal, Dr. Parrott said, it should have "a beneficial effect on the professional liability situation in the long run."

MEDICAID SERVICES STATE BY STATE,

JUNE 1, 1976 √

* BASIC REQUIRED MEDICAID SERVICES: Every Medicaid program must cover at least these services for at least everyone receiving federally supported financial assistance: inpatient hospital care; outpatient hospital services; other laboratory and X-ray services; skilled nursing facility services and home health services for individuals 21 and older; early and periodic screening, diagnosis, and treatment for individuals under 21; family planning; and physician services. Federal financial participation is also available to States electing to expand their Medicaid programs by covering additional services and/or by including people eligible for medical but not for financial assistance. For the latter group States may offer the services required for financial assistance recipients or may substitute a combination of seven services.

Services provided only under the Medicare buy-in or the screening and treatment program for individuals under 21 are not shown on this chart.

Definitions and limitations on eligibility and services vary from State to State. Details are available from local welfare offices and State Medicaid agencies.

● offered for people receiving federally supported financial assistance

\+ offered also for people in public assistance[2] and SSI[3] categories who are financially eligible for medical but not for financial assistance

FMAP[4]	BASIC* REQUIRED MEDICAID SERVICES SEE ABOVE		Additional services for which Federal financial participation is available to States under Medicaid. Clinic services	Prescribed drugs	Dental services	Prosthetic devices	Eyeglasses	Private duty nursing	Physical therapy and related services	Other diagnostic, screening, preventive and rehabilitative services	Emergency hospital services	Skilled nursing facility services for patients under 21	Optometrists' services	Podiatrists' services	Chiropractors' services	Care for patients 65 or older in institutions for mental diseases	Care for patients 65 or older in institutions for tuberculosis	Care for patients under 21 in psychiatric hospitals	Institutional services in intermediate care facilities	
74	●	Alabama		●		●	●				●	●	●				●		●[5]	AL
50	●	Alaska					●				●	●	●			●		●	●[5]	AK
60		Arizona																		AZ
75	+	Arkansas	+	+	+	+					+	●			+	+	+	+	●[5]	AR
50	+	California	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+[5]	CA
55	●	Colorado		●		●		●			●	●		●		●		●	●[5]	CO
50	+	Connecticut	+	+	+	+	+	+	+	+		+	+	+	+	+		+	+[5]	CT
50	●	Delaware	●	●				●						●		●	●		●	DE
50	+	D.C.	+	+		+	+		+	+	+	+	+	+		+	+	+	+[5]	DC
57	●	Florida		●							●					●	●		●[5]	FL
66	●	Georgia	●	●		●				●		●		●		●	●		●[5]	GA
50	+	Guam	+	+	+	+	+		+		+	+	+							GU
50	+	Hawaii	+	+	+	+	+		+	+	+	+	+						+	HI
68	●	Idaho	●	●							●	●	●	●	●				●[5]	ID
50	+	Illinois	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+[5]	IL
57	●	Indiana	●	●	●	●	●	●	●	●	●	●	●	●	●	●		●	●	IN
57	●	Iowa		●	●	●	●		●		●	●	●	●	●				●[5]	IA
54	+	Kansas	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+[5]	KS
71	+	Kentucky	+	+	+	+			+		+	+				+	+	+	+[5]	KY
72	●	Louisiana	●	●		●				●	●	●			●	●	●	●	●[5]	LA
71	+	Maine	●	+		+		+	+	●	+			+	+	+		+	●[5]	ME
50	+	Maryland	+	+		+	+				+		+			+	+		+[5]	MD
50	+	Massachusetts	+	+		+	+	+	+	+	+	+	+	+		+	+		+[5]	MA
50	+	Michigan	+	+		+				+	+	+		+	+	+	+	+	+[5]	MI
57	+	Minnesota	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+[5]	MN
78	●	Mississippi		●	●							●				●	●		●[5]	MS
59	●	Missouri		●	●						●		●			●	●		●[5]	MO
63	+	Montana	+	+	+	+	+	+	+	+	+	+	+	+		+		+	+[5]	MT
56	+	Nebraska	+	+	+	+	+	+	+		+	+	+	+	+	+	+		+[5]	NB
50	●	Nevada	●	●	●	●	●	●	●		●	●	●	●	●	●			●[5]	NV
60	+	New Hampshire	+	+		+	+	+	+	+	+	+	+	+	+	+			●[5]	NH
50	●	New Jersey	●	●	●	●	●		●	●	●	●	●	●	●	●	●	●	●	NJ
73	●	New Mexico	●	●	●	●	●	●	●		●	●	●	●					●[5]	NM
50	+	New York	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+[5]	NY
68	+	North Carolina	+	+	+		+			+		+	+	+	+	+	+	+	+[5]	NC
58	+	North Dakota	+	+	+	+	+	+	+	+	+	+	+	+	+			+	+	ND
54	●	Ohio	●	●	●	●	●	●	●	●	●	●	●	●	●	●		●	●[5]	OH
67	+	Oklahoma		●	+									+		+		+	+[5]	OK
59	●	Oregon	●	●	●	●	●	●			●	●	●	●	●	●	●	●	●[5]	OR
55	+	Pennsylvania	+	●	●	●	+				+	+	+	●	+	+		+	+[5]	PA
50	+	Puerto Rico	+	+	+			+	+	+	+						+			PR
57	+	Rhode Island		+	+	+	+						+	+		+			●[5]	RI
74	●	South Carolina	●	●	●	●	●		●		●	●	●		●	●	●	●	●[5]	SC
67	●	South Dakota	●	●		●	●		●		●	●	●	●	●				●[5]	SD
70	+	Tennessee	+	+		+					+					+	+	+	+[5]	TN
64	●	Texas		●	●		●				●		●	●			●		●[5]	TX
70	+	Utah	+	+	+	+	+	+	+		+	+	+	+	+	+		+	+[5]	UT
70	+	Vermont	+	+		+					+	+		+		+		+	+[5]	VT
50	+	Virgin Islands	+	+	+	+	+													VI
58	+	Virginia	+	+			+		+		+	+	+	+		+	+		+[5]	VA
54	+	Washington	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+[5]	WA
72	+	West Virginia	+	+	+	+	+	+	+			+	+	+	+	+	+		+	WV
60	+	Wisconsin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+[5]	WI
61	●	Wyoming										●	●						●	WY
● 21	●		13	21	12	14	12	5	10	5	18	18	15	14	10	14	11	8	25	
+ 32	+		29	30	22	27	24	14	22	17	25	25	23	23	18	27	19	21	25	
53	Total		42	51	34	41	36	19	32	22	43	43	38	37	28	41	30	29	50	

Intermediate Care Facilities (ICF): P.L. 92-223 transferred the ICF program to Medicaid (Title XIX) as an optional service, effective 1-1-72. States may at their option include institutions for the mentally retarded, both public and private. See footnote five.

1/ Data from Regional Office reports of characteristics to State programs and State plan amendments.

2/ People qualifying as members of families with dependent children (usually families with at least one parent absent or incapacitated).

3/ People qualifying as aged, blind, or disabled under the Supplemental Security Income program.

4/ FMAP - Federal Medicaid Assistance Percentage: Rate of Federal financial participation in a State's medical vendor payment expenditures on behalf of individuals and families eligible under Title XIX of the Social Security Act. Percentages, effective from July 1, 1975, through June 30, 1977, are rounded.

5/ Including ICF services in institutions for the mentally retarded.

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Organo Oficial Fundado en 1903

Volumen 68 Septiembre 1976 Número 9

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PORTADA: Vista del Viejo San Juan (Calle Cristo esq. Sol)
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THE PREVENTION OF CORONARY ARTERY DISEASE THROUGH THE CONTROL OF HYPERTENSION: A PERSPECTIVE

Elí A. Ramírez, MD, M.Sc (IM), FACP

Two of the most significant developments of the last twenty years in the cardiovascular field have been related to hypertension. The first is the determination of the crucial role of hypertension as a pathogenetic factor in cardiovascular disease. The second is the discovery that the vast majority of its complications can be prevented by relatively simple treatment.

The possibility of preventing coronary artery disease through the treatment of hypertension is one of the most important challenges to medicine today. Many factors besides hypertension have been linked to atherosclerosis including clotting-fibrin abnormalities, trace metal metabolic defects, vitamin deficiencies, sex, salt ingestion, body build, dietary factors, obesity, physical inactivity, hormonal imbalances, heredity, smoking, hyperlipidemia, personality and diabetes. However, only a few of these are amenable to correction; namely hypertension, obesity, hyperlipidemia, smoking, physical inactivity, dietary factors, and perhaps personality. From a practical standpoint, hypertension is probably the most important because it is the most prevalent, it is probably the most harmful, it is one of the easiest to detect, and is perhaps the easiest to control. The possible impact on the general population of the prevention of atherosclerosis through the treatment of hypertension can be estimated from the finding by the National Health Survey (1), that from 15 percent to 20 percent of American adults have a blood pressure of 160/95 mm. Hg or above.

Numerous observations and experiments (2) have corroborated that hypertension gives rise to atherosclerosis. In coarctation of the aorta, atherosclerosis of the coronary arteries and of the aorta is common above the level of obstruction where the pressure is lower. The chemical changes precursor to atherosclerosis regularly appear in the aortic wall of experimental animals when aortic coarctation is created artificially. In renal arterial obstructive disease, the renal arteries protected from the systemic hypertension by the obstructive lesion are free of atherosclerosis, while those of the contralateral kidney are markedly affected. Correction of the renal arterial obstruction results in atherosclerosis of the previously normal arteries if the hypertension persists, but not if the hypertension is cured. An extraordinarily high prevalence of coronary sclerosis is commonly observed in children with supravalvular aortic stenosis with aortic hypoplasia; a condition in which the coronary arteries are subjected to high levels of pressure. The pulmonary arteries never develop atherosclerosis unless there is pulmonary hypertension concomitantly. In experimental animal models including dogs, rabbits, rats and primates, atherosclerotic changes such as increased thickness and rigidity of arterial wall, hyperplasia and hypertrophy of smooth muscle cells, increase in the arterial content of calcium and other minerals, increase in collagen and elastic fibers, etc., have been regularly induced when the animals have been made hypertensive. Conversely, it has been shown that these changes can be prevented or reversed by antihypertensive drugs (3, 4). Several human autopsy studies (5, 6) have shown that hypertensives manifest a much higher incidence of coronary atherosclerosis than normotensives.

Experimental investigations have given insight into the production of atherosclerosis by hypertension but the specific mechanism has not been elucidated. The change in lateral wall pressure and tension and the altered gradients in blood velocity are stressful to the vessel wall. The available evidence indicates that this stress stimulates the changes in connective tissue, metabolism and endothelial permeability which are associated with atherosclerosis. It has been postulated that lipids may percolate into the arterial wall as a result of the increase in pressure. Several hormonal

Presented in part at the American College of Chest Physicians post graduate course on Ischemic Heart Disease, San Juan, P. R. Dec. 5, 1975.

substances and chemical mediators of injury known to be altered in hypertension such as serotonin, histamine, epinephrine, proteolytic enzymes, renin, angiotensin, catecholamines, and mineralocorticoids can also accelerate the processes precursor to atherosclerosis.

On the clinical side, the results of a number of epidemiological investigations (6, 7) have shown that the risk of every manifestation of coronary heart disease including angina, myocardial infarction and sudden death is significantly related to the antecedent level of systolic and diastolic blood pressure. The Framingham experience (8) showed that smoking is associated with an increased risk for atherosclerosis in a 2:1 ratio, hypercholesterolemia with a ratio of approximately 3:1, and hypertension with a ratio of 4:1. Most important is the observation that hypertension is apparently an independent pathogenetic factor by itself, and that multiple risk factors are additive in terms of increased risk.

With this background we would have reason to look forward hopefully to the prevention of coronary atherosclerosis through the treatment of hypertension. However, this evidence has not been forthcoming in humans studies. The Veterans Administration studies (9) presented convincing evidence that antihypertensive treatment prevents complications in mild and moderate hypertensive patients (See Table I). Congestive heart failure, stroke, and progressive renal damage were sharply reduced or eliminated in subjects treated with active drugs. However, the incidence of myocardial infarction was the same in the actively-treated and placebo-treated groups, although sudden death was slightly more frequent in the placebo-treated group.

The inability to demonstrate conclusively a significant effect of antihypertensive treatment on the incidence of myocardial infarction is not necessarily inconsistent with the clinical and experimental evidence that hypertension causes and accelerates atherosclerosis. A large proportion of the sample of patients in the Veterans Administration Study was over 50 years of age, and more than half presented with renal or cardiovascular abnormalities. The study had to be terminated within a relatively short period of time because of ethical considerations due to the high incidence of complications in the control group. If the age group had been younger, the sample larger, and the follow up longer, the possibility of demonstrating the reversibility of a chronic process such as atherosclerosis would have been improved. More work is needed in determining the effect of long range antihypertensive therapy on younger patients and in females. The question of whether it makes a difference to treat hypertension early, before complications appear, rather than to wait until they are imminent, has to be answered. This may

TABLE I: Morbid Events by diagnostic categories observed in control and actively treated mild - moderate hypertensives in the Veterans Administration Cooperative Study (9)

	CLASSIFICATION OF MORBID EVENTS BY DIAGNOSTIC CATEGORIES			
	Total Events		Terminating Events	
Diagnosis	Control	Treated	Control	Treated
Cerebrovascular accident	20	5	12	1
Coronaryartery disease	13	11	11	6
Congestive heart failure	11	0	5	0
"Accelerated" hypertension	4	0	4	0
Renal damage	3	0	1	0
Other	5	6	2	2
Total	56	22	35	9

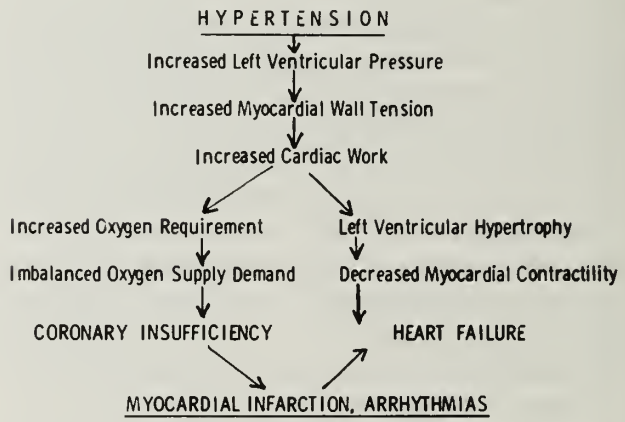


Figure 1: *Mechanism of the adverse effect of hypertension upon the myocardium.*

be the principal issue in the atherosclerotic preventive role of antihypertensive treatment. The problem of reversibility of advanced atherosclerotic lesions requires further investigation. Such studies are now in progress (10).

From the point of view of the management of the hypertensive patient with established atherosclerotic heart disease, there is definite evidence that considerable benefit accrues to the removal of the mechanical effect of the hypertension (See Figure 1). The increased arterial pressure results in increased myocardial wall tension and cardiac work, which in turn produces increased oxygen consumption. This may lead to an imbalance between the supply and the demand for oxygen which may result in all the complications of coronary insufficiency including myocardial infarction, arrhythmias and congestive heart failure. The increase in wall tension also produces ventricular hypertrophy which aggravates the oxygen demand. This may establish a vicious cycle since increased oxygen demand may in turn produce ventricular hypertrophy. The ventricular hypertrophy also decreases the contractility of the myocardium which predisposes to heart failure as well.

Heart failure in hypertensives frequently results from an interaction of hypertension and atherosclerosis, although it may complicate hypertension alone. In one series (11), the five year survival of patients with angiographically proven coronary lesions was reported to be 73 percent in normotensive subjects and 61 percent in hypertensives. When congestive heart failure was present the five year survival was only 38 percent. The adverse effect of the combination of hypertension and atherosclerotic coronary artery disease is obvious.

It is clear from numerous reported observations that congestive heart failure is not only preventable by antihypertensive treatment, but may be reversed as well. In the already cited Veterans Administration study of mild to moderate hypertensives, congestive heart failure occurred in 11 of 194 placebo treated patients and in none of 184 patients treated with active drugs. The fact that these results were obtained within an average follow up period of only 3.2 years indicates that antihypertensive therapy can be of immediate benefit in hypertensives with coronary atherosclerosis regardless of the possible long range benefit on the coronary arterial lesion itself.

Summary

1. There is evidence that hypertension causes and aggravates coronary artery disease in man. However, there is no conclusive evidence at present that prophylactic antihypertensive therapy prevents myocardial infarction.

2. There is no question that antihypertensive therapy effectively prevents and reverses congestive heart failure and symptomatic coronary insufficiency in hypertensive subjects.

3. Hypertension is but one of the factors concerned in the pathogenesis of atherosclerosis. Other reversible factors such as obesity, physical inactivity, smoking, personality, and hyperlipidemia should also be controlled. Nevertheless, the results of efforts to change smoking, dietary, and social behavior patterns on a long-term basis have been generally disappointing. In a recent study (12), the education of patients produced no significant changes in the prevalence of risk factors for atherosclerosis. On the contrary, it seemed that those patients who were subjected to the educational effort became antagonistic and withdrew from follow up. Another approach, the prophylaxis of atherosclerosis through hypocholesterolemic drug therapy, has not resulted in significant benefit (13).

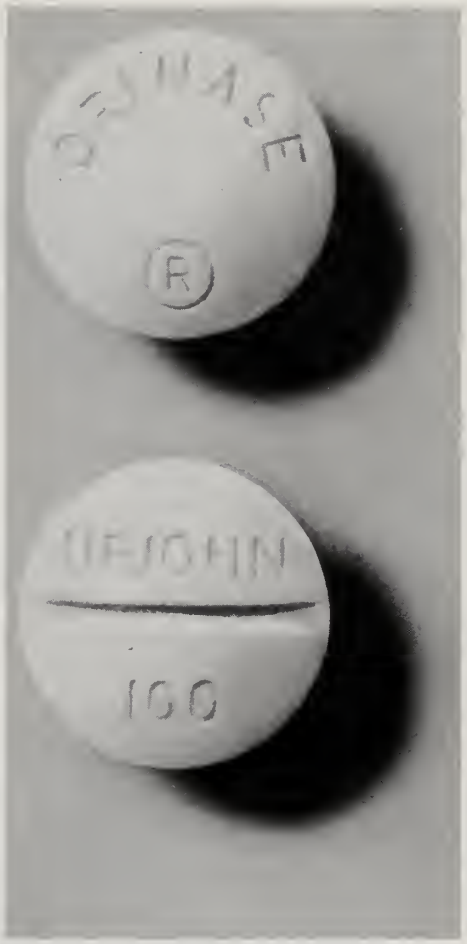
Thus, the treatment of hypertension because of its high prevalence, its high hazard as a risk factor, its easy diagnosis, and its simple management at little expense may actually represent our most effective approach to the prevention of atherosclerosis. Additional investigations are required to resolve this question in its multiple aspects, and to determine if the benefits of treatment outweigh the hazards of the medications now available for this purpose.

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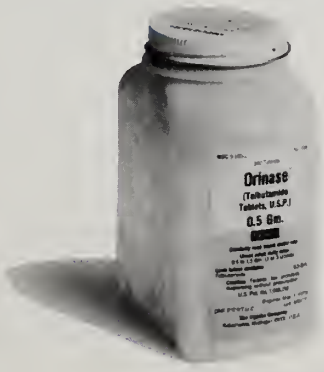
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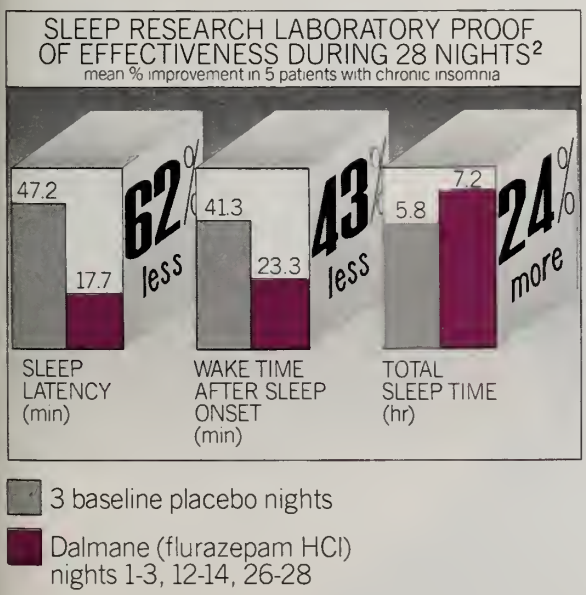
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Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

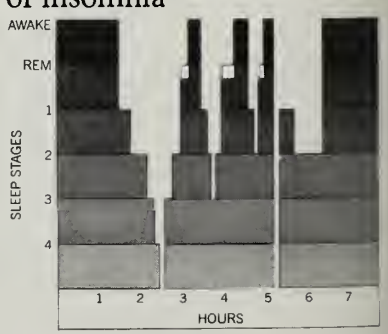
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LUNG TRANSPLANTATION: IMPROVED SURVIVAL OF CANINE LUNG ALLOGRAFTS PERFUSED WITH ANTITHYMOCYTE GLOBULIN (ATG)

Luis H. Toledo-Pereyra, MD, PhD *
Richard M. Condie
Toni Hau, MD
Richard L. Simmons, MD
John S. Najarian, MD

Prolongation of organ allografts has generally required the use of systemic immunosuppressive drugs in order to modify the host's reactivity to the histocompatibility antigens on the graft. The opposite approach, that of altering the grafted tissues themselves so that the histocompatibility antigens of the tissue are not recognized by the host, has received comparatively minimal attention. Our preliminary data indicated that antilymphocyte globulin (1) and other drugs (Concanavalin A (2), phytohemagglutinin-M (2), dipyrimadole (3), chondroitin sulphate (4)) can modify the immunogenicity of canine kidney allografts. In this paper we study the modification of graft antigenicity on lung allografts perfused with ATG before transplantation into mildly immunosuppressed recipients.

Material and Methods

Mongrel dogs of either sex, weighing between 20 to 28 kg for the donor or recipient animals, were anesthetized with sodium methohexital for induction and Fluothane (R) for maintenance. Oxygen was continuously used during ventilation given through an endotracheal tube. In the donor animal, the left lung was excised through a thoracotomy incision at the 5th intercostal space. The left pulmonary artery, bronchus and atrial cuff were carefully dissected out by avoiding any excessive handling, instrumental trauma and leaving enough length for a satisfactory anastomosis. Subsequently, the lung was removed and flushed, through the pulmonary artery with 500 ml of silica gel fraction (SGF) of plasma (5) at 15° C and 40 cm. of water. Donor and recipient dogs received Ringer's lactate solution as intravenous therapy during surgery. The left thorax of the recipient was opened in similar way as in the donor animal. The left lung was excised in such a manner as to preserve ample tissue for the anastomosis. A single lumen was made of the pulmonary veins at the level of the atrium. The atrial cuff anastomosis was performed with one layer of over-and-over suture (6-0 cardiovascular Tevdek) of intima-to-intima approximation. The pulmonary artery was anastomosed next with 5-0 cardiovascular Tevdek in a routine fashion. Finally, the bronchus sutured with 3-0 Mersilene, the anterior wall was secured from within the lumen with a continuous everting mattress suture to create air-sealed mucosal approximation, and the posterior wall was inflated frequently before the thoracotomy was closed. A chest tube placed in at the end of the procedure, was removed two hours after surgery.

On the day of surgery, and daily for 3 days thereafter, the animals were given intravenously 1 L of Ringer's lactate solution, 2 ml/L of Vitamin B complex, 1 gm/L of Vitamin C and 500mg/L of chloramphenicol. In some circumstances, canine plasma was given during the operation or immediately thereafter, in order to replace blood volume loss. Oral feeding was allowed until the 2nd day post transplantation. Regular diet was progressively administered. On the 3rd post-operative day, a right thoracotomy was performed and the pulmonary artery of the non-transplanted lung was ligated with 2-0 Tevdek suture. This procedure allows us to test the capacity of the transplanted lung on maintaining by itself the survival of the animal with contralateral pulmonary artery ligated. All dogs except Group V were kept on azathioprine, 5-0 mg/kg per day, for the first 3 days and then 2.5 mg/kg per day until death. Blood gases, complete blood count and chest x-ray were obtained 1 hour post grafting and daily for the first 3 days and then every 4 days until death or sacrifice. Postmortem examination was performed in all dogs and microscopic specimens were obtained from both their own and the transplanted lung. All dogs that died as a result of obvious technical errors were eliminated from the study.

The ATG was prepared by immunizing goats with bimonthly injections of $2x10^8$ dog thymus lymphocytes over a total period of 3 months. After absorption with dog red blood cells the antithymocyte serum was purified with 40 percent

From the Department of Surgery, University of Minnesota Health Sciences Center, Minneapolis, MN 55455.

This work was supported by USPHS Grant No. AM 13083.

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TABLE I
SURVIVAL OF DOGS WITH LUNG ALLOGRAFTS AFTER PERFUSION WITH ATG

Groups	No. Dogs	Perfusate	Perfusate Treatment	Mean Survival ± SE (Days)
I	6	SGF	None	5.3± 3.2
II	6	SGF	ATG (1 gm/L)	13.4± 4.7 *
III	6	SGF	ATG (750 mg/L)	10.1± 5.0 **
IV	6	SGF	ATG (500 mg/L)	8.2± 3.4
V	6	SGF	ATG (1 gm/L)	6.5± 3.8

* $p < 0.01$ when Group II compared to control group (1).

** $p < 0.08$ when Group III compared to control group (1). Recipient dogs from Groups I, II, III, and IV, received azathioprine 5 mg/k/day for 3 days, then 2.5 mg/k/day until death. Group V dogs received no immunosuppression.

$(NH_4)_2 SO_4$ followed by fractionation on QAE ion exchange column and elution at various pH levels (7.0 - 4.0). ATG at doses of 50 mg/kg prolonged the survival of canine skin grafts up to 22 days and reversed delayed sensitivity. ATG in vitro maintained a lymphocytotoxicity titer against peripheral blood lymphocytes of 1:32,000 and a hemagglutination titer <1:64.

All donor animals received 1 gm each of methylprednisolone and 2000 U of sodium heparin intravenously 30 min before the vascular clamps were placed on. Five groups of 6 recipient dogs each (30), were studied. Group I dogs received lung transplants perfused with SGF without any drugs in the perfusate. Group II, III and IV lungs were perfused with ATG, 1 gm/L, 750 mg/L and 500 mg/L respectively. Group V lungs were perfused with ATG, 1 gm/L without immunosuppression to the recipient. Statistical analysis with standard error and Student T-test was determined for all parameters between groups of animals.

Results

Table I shows the survival of all dogs with lung allografts. The perfusion of the donor lung with SGF did not prolong the survival of lungs in recipient dogs with mild immunosuppression. Similar results were observed in dogs transplanted with lungs perfused with ATG that had no immunosuppression. Statistically significant prolongation of survival was observed in mildly immunosuppressed recipients of lungs perfused with high concentrations of ATG (1 gm/L). Dogs transplanted with lungs perfused with lesser concentration of ATG (750 mg/L-500 mg/L) had a less prolonged survival than those of higher doses; it was however, considerably longer than the control animals ($p < 0.08$).

Dogs transplanted with lungs perfused with high concentrations of ATG (750 mg-1.0 gm/L) had no significant modification in blood gases or in the ventilatory pattern in the immediate post-operative period. The white blood cells increased to over 25,000 with granulocytosis, the hematocrit decreased to 35 average and the platelets were in the low normal limits the first 5 days after transplant. Thereafter, the blood parameters remained within normal limits. On the second week after surgery, there was a progressive decrease of the arterial PO_2, slow increase of the arterial blood PCO_2 and decrease of the minute tidal volume. At the end of this week, the respiration was slow with a maximum inspiratory effort and prolonged expiration indicating terminal respiratory distress (Table II).

Dogs transplanted with lungs perfused with low doses of ATG (500 mg/L), control animals and those dogs perfused with ATG without recipient immunosuppression, had an immediate response after surgery similar to the previous groups. However, in the first 72 hours post-operatively, clinical and laboratory signs of hypoxia with CO_2 retention were noted. The hematocrit fell down to 28 and the white blood count increased to 32,000 with severe granulocytosis. At the end of the first week practically all dogs died with the usual clinical picture of terminal respiratory

TABLE II
BLOOD GASES PATTERN AFTER LUNG TRANSPLANTATION (Average Values)

Groups		Post operative Day 1	3	5	7	10	14
I (Control)	pH	7.48	7.43	7.34	7.30	—	—
	pO_2	97	85	70	62	—	—
	pCO_2	30	33	41	50	—	—
II (ATG 1gm/L)	pH	7.45	7.46	7.44	7.41	7.42	7.38
	pO_2	95	90	88	85	75	62
	pCO_2	28	30	32	34	39	47
III (ATG 750 mg/L)	pH	7.46	7.43	7.41	7.42	7.38	7.30
	pO_2	94	91	85	80	70	59
	pCO_2	31	29	32	38	41	48
IV (ATG 500 mg/L)	pH	7.44	7.47	7.41	7.38	7.33	—
	pO_2	96	92	86	76	58	—
	pCO_2	29	33	34	36	45	—
V (ATG 1 gm/L)	pH	7.47	7.48	7.39	7.33	—	—
without immunosuppression)	pO_2	95	84	72	65	—	—
	pCO_2	28	32	39	46	—	—

distress.

The rejection phenomena varied in intensity in the different group of animals. No uniform pattern was evident. It basically consisted of an initial perivascular infiltration of mononuclear cells, alveolar involvement and subsequent obliteration of alveolar spaces. These microscopic findings have been previously reported by several groups dealing with experimental lung transplantation (6, 7). In several animals, pneumonia coexisted with rejection. Hemorrhagic necrosis was observed only in one of the control dogs. Microscopic pulmonary edema was present in all animals, except 3 dogs in Group II, 2 animals in Group III and one dog in Group IV.

The causes of death for all transplanted lung dogs are noted in Table III. Five dogs were eliminated from the final analysis because of technical failures which occurred during surgery. This included one technical post-operative bleeding, one anesthesia overdosage, one bronchoaspiration and two of acute pulmonary edema due to fluid overload.

Discussion

These experiments demonstrate that perfusion of dog lungs with high doses of ATG will allow mildly immunosuppressed dogs to maintain these grafts for long periods of time. Low doses of ATG did not prolong the survival of mildly immunosuppressed lung allografts.

Two possible mechanisms could be invoked in the reduction of immunogenicity of lung allografts perfused with ATG. First, the destruction or neutralization of passenger leukocytes with ATG, so these lymphocytes cannot proliferate or be active in the host animal, therefore, decreasing the antigenic challenge. Second, the masking of graft antigens by nonspecific binding of goat globulin to lung cells, thus preventing the host from identifying the masked antigens.

Attempts have been made to "mask" alloantigens on grafts by either specific or nonspecific serologic pretreatment. Such attempts have included antilymphocyte

TABLE III
CAUSE OF DEATH OF LUNG ALLOGRAFTS AFTER PERFUSION WITH ATG

Cause of Death	GROUPS I	II	III	IV	V
Pneumonia	2	1	1	1	2
Sepsis	1	0	1	0	1
Atrial Thrombosis	1	0	0	1	1
Pulmonary Edema	1	0	1	1	1
Pulmonary Artery Thrombosis	0	1	1	1	0
Rejection	1	2	1	1	1
Lung Fibrosis	0	1	1	0	0
Bronchial Stenosis	0	1	0	1	0

serum (ALS) and specific alloantiserum, including F (ab) fragments. Antilymphocyte serum has been utilized both to pretreat the graft donor (perhaps leading to reduction in passenger leukocytes) and the graft itself. Guttman and associates (8, 9), pretreated rat donors with rabbit anti-mouse thymus IgG: kidneys from these rats had prolonged survival. Cerilli and co-workers (10) failed to confirm Guttman's results with dog kidney allografts and horse anti-dog ALG. Confirmatory reports have also been made using skin grafts, tumor grafts, corneal allografts, and rat heart allografts (11). Iwahashi and colleagues (12) failed to get prolongation of dog lung allografts with horse anti-dog lymphocyte serum followed by transplantation into minimally immunosuppressed hosts.

Alloantisera have similarly been used in an attempt at specific blocking or masking the alloantigens on grafts. This approach has gained new credibility because of the recent finding that antibodies can "block" the cell-mediated cytotoxicity of specifically sensitized lymphocytes in tissue culture. The literature in this field has recently been reviewed by the Hellstroms (13). There is however, considerable literature on the use of alloantiserum or alloantiglobulin for the pretreatment of grafts before allotransplantation, and some success has been reported for allogenic tumor cells and skin grafts.

Our results suggest that lung graft antigen modification with ATG (high doses) may supplement immunosuppression in the prolongation of lung allografts. The mechanisms are still unknown and are a subject for further investigation.

Summary

Canine lungs perfused with high doses of ATG (1 gm/L) prolonged the survival of moderately immunosuppressed recipients without interfering with graft function. Lower doses of ATG (750-500 mg/L) determined a lesser prolongation of lung allograft survival. There was no prolongation of graft survival in those animals transplanted with lungs perfused with ATG that received no immunosuppression. Thus, these results suggest that lung graft antigen modification with ATG may supplement immunosuppression in the prolongation of lung allograft survival.

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SURGICAL RECONSTRUCTION OF LIDS FOR CANCEROUS AND OTHER LESIONS FIRST DR. ANTONIO NAVAS MEMORIAL LECTURE

Guillermo Picó, MD

Permit me to express my appreciation to the Board of Directors of the Section of Ophthalmology of the Puerto Rico Medical Association in granting me the opportunity to deliver the first Antonio Navas Memorial Lecture. I feel deeply the responsibility as well as the honor of the selection.

At this moment we are here together to do homage to the memory of a very distinguished Puerto Rican ophthalmologist, Dr. Antonio Navas. We have all listened to Dr. Manuel Miranda's description of doctor Navas' productive life. Let me add some thoughts of my own.

I had the privilege of meeting doctor Navas very early in my professional career, when as an intern at Presbyterian Hospital in San Juan I trained under him at the clinics and the operating room. I admired his dedication to his patients, his skill in both diagnosis and surgery. His introduction to our specialty instilled in me a preference for this field. Upon my return from the Mainland, as a qualified ophthalmologist, I worked part-time at the San Juan City Hospital, with doctor Navas heading the Service of Ophthalmology. Since that time, I witnessed again the devotion of doctor Navas to his work, his kindness to his patients and the application of best medical and surgical methods.

When I was appointed Department Head of Ophthalmology at the University of Puerto Rico School of Medicine in 1952, he offered all his cooperation and as the years went by, he fulfilled this offer by contributing greatly to the teaching of undergraduate medical students and our residents alike. Even after being seriously ill, for a period of years, doctor Navas continued attending the clinics and the operating room. He was a great example to all of us and we still miss him. I remember him as an outstanding ophthalmologist, a great human being and my very good friend.

Presented at the Annual Meeting of the Section of Ophthalmology of the Puerto Rico Medical Association, July 26, 1975.

Request reprints from: Guillermo Picó, MD, 1475 Wilson Avenue, Santurce, Puerto Rico.

General Considerations

In this presentation I will omit the description of the numerous procedures for repair and reconstruction of the lids, all or most having merits. There are different technics of reconstructing lids and in my opinion the best procedure in each individual case is the one which the particular surgeon is most familiar with. I will limit myself in this paper to present an outline of the approach I have found useful and successful in reconstruction of lids in the surgical management of different, especially malignant, lesions.

The main lesions of lids requiring extensive surgical intervention are: congenital coloboma, traumatic partial loss of lids, cicatricial ectropion, and benign or malignant neoplasms.

As Reese mentioned (1), the large majority of lid carcinomata are best treated by surgical excision followed by plastic repair. The extension of the lesion should be determined by careful inspection and palpation. The excision should extend at least three millimeters beyond the limits of the tumor. Use of radiation ought be limited to cases of far advanced cancer of lids requiring a combination of radiation and surgery or for patients with far advanced inoperable carcinoma of the lids where radiation is the only possible choice.

Surgical Management

The lesions in the lids can be divided into cases involving only the skin and those including skin and lid margins. Small benign lesions like verrucae or papillomata, or early small malignant neoplasms of only the skin of the lids, are easily handled by an excision of the lesion and closing the defect by suturing horizontally the edges of the defect with interrupted silk sutures. When the area is more extensive as found in malignancies or a cicatricial ectropion, the removal of the tumor or of the subcuta-

neous scar tissue in a cicatricial ectropion, results in a defect that requires skin taken from other sources. I used a skin graft from the unaffected lid or from the post-auricular area in the past, but I have mostly discarded this procedure and use instead, with better results, a horizontal sliding skin flap (Figs. 1, 2, 3, 4, 5). The scars of the horizontal incisions gradually fade away and disappear into the contour lines of the face, while skin grafts from other surfaces frequently show more cosmetic blemishes and differ in color.

Whether the lesion involves only the skin or also the lid margin, the excision should be made in square or rectangular shape. If the lesion affects only the skin, the sliding flap from the temporal region will be rectangular, but when the margin is also involved, the upper incision ought be inclined upwards and temporally for a short distance after leaving the outer



Figure 1: *Cicatricial ectropion of left lower lid.*



Figure 2: *Sliding skin flap used to correct cicatricial ectropion. Appearance before removal of sutures.*



Figure 3: *Final results 18 months following surgery for cicatricial ectropion.*

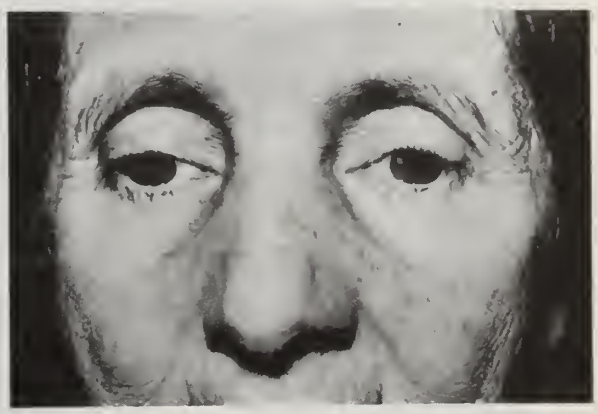


Figure 4: *Basal cell carcinoma in skin of left lower lid.*

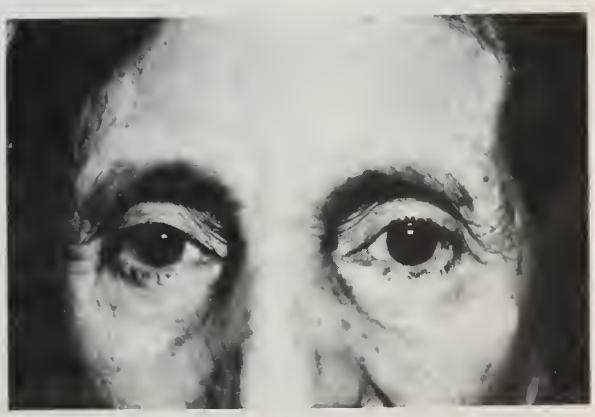


Figure 5: *Final results 9 months after excision of basal cell carcinoma and repair with sliding horizontal flap.*

canthus and then proceed towards the temporal area in a straight line. The lower lid is easier repaired than the upper, since the room available for the horizontal sliding flap is greater in the lower than in the upper lid.

I agree with Fox (2) that skin tumors of the medial canthi must be well excised and the area left to granulate and heal by second intention without sutures or skin grafts (Figs. 6, 7).

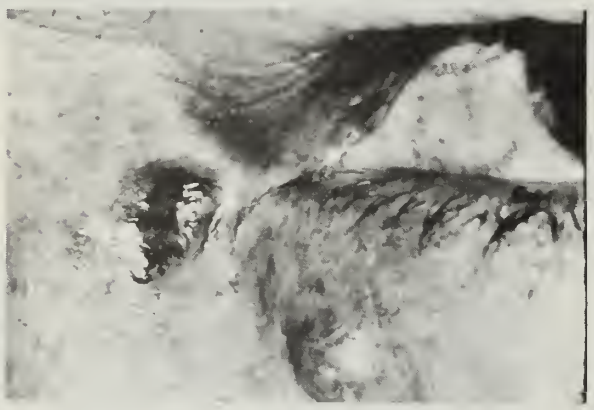


Figure 6: *Basal cell carcinoma in the skin of the medial canthal area of the left eye.*

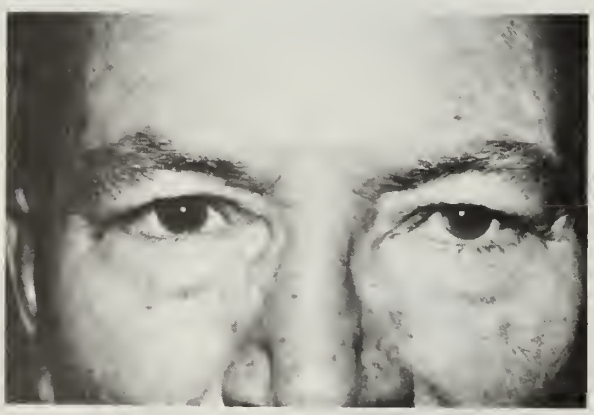


Figure 7: *Appearance of patient one year later.*

Repair of either lid, when the defect of the margin is about 25 percent of the original lid length may be fashioned by direct border to border approximation in two layers (Figs. 8, 9).

Restoration of the lower lid when the margin defect extends between 25 percent and 80 percent of the



Figure 8: *Congenital coloboma of right upper lid.*



Figure 9: *Appearance one year after the repair.*

original lid length may be accomplished with a horizontal sliding flap (Figs. 10, 11, 12, 13). Should the defect of the upper lid margin measure between 25 percent and 50 percent of the original lid length, a horizontal rectangular sliding flap (Figs. 14, 15) may be used.

Certain important points in lid reconstruction by horizontal skin flaps should be emphasized:

1. The excision of the lesion, whether involving the skin alone or also the margin of the lid, is to be made by removal of the desired amount of tissue in square or rectangular shape.

2. A lateral canthotomy is performed by inclining the upper skin incision slightly upward, to follow the contour of the lower lid.

3. A cantholysis is performed by severing with scis-



Figure 10: *Basal cell carcinoma in skin and margin of left lower lid.*



Figure 11: *Appearance 18 months after excision of tumor in skin and margin of left lower lid and reconstruction with horizontal sliding flap.*



Figure 12: *Basal cell carcinoma in skin and margin of left lower lid.*

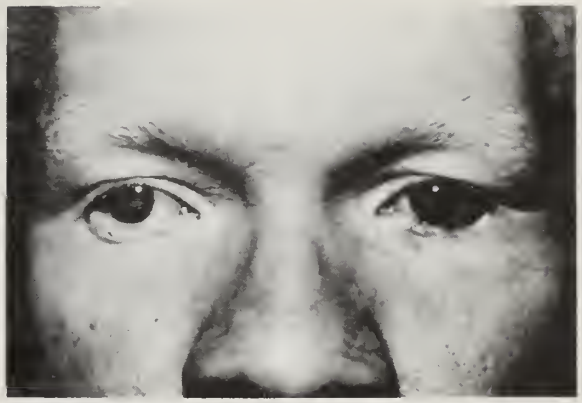


Figure 13: *Appearance two years after excision of tumor in skin and margin of left lower lid and reconstruction with horizontal sliding flap.*



Figure 14: *Traumatic coloboma of medial half of right upper lid.*

sors the corresponding lower or upper portions of the lateral canthal tendon. This permits a displacement of the lateral part of the lid and the new segment to be added to the lid toward the nose and allows the defect to be closed.

4. The maximal part of the palpebral conjunctiva is salvaged.

5. The sliding graft participating in the new part of the lid must be thin.

6. Neither "halving" nor intermarginal adhesions are required.

7. The temporal sliding flap should be sufficiently undermined to permit a comfortable sliding of the graft to fill the defect.

8. Several 4-0 and many 6-0 silk sutures are applied between the sliding flap and neighboring tissues fixing it in position.



Figure 15: *Appearance of right upper lid 18 months after correction of traumatic coloboma with use of horiziontal sliding flap.*

9. The conjunctiva from the fornix is mobilized and sutured with interrupted 6-0 silk sutures to the border of the mobilized skin from the temporal region so as to line the new segment of the lid.

10.With the horizontal sliding flap as well as with the Mustardé rotating cheek flap (3), the size of the repair added to the margin of the reconstructed lid is calculated by substracting from the length of the defect 25 percent of the original length of the lid.

11.I have found it unnecessary to add nasal cartilage and mucosa to the new lid addition; skin and conjunctiva suffize.

12.As I have mentioned before, this technic can be used for repair of up to 80 percent of the lower lid but not for more than 50 percent of the upper lid.

When the defect in the lower margin measures more than 80 percent of the original lid length, a Mustardé rotating cheek flap (Figs. 16, 17) may be used. When the defect in the margin of the upper lid extends from 50 percent to 100 percent of the original lid length, it requires a Cutler-Beard flap from the lower lid (Figs. 18, 19).

Technical details of the reconstruction by the use of a Mustardé rotating cheek flap can be found in Callahan (4) but Mustardé (3, 5, 6) has stressed certain important points:

1. Excision of inverted triangle is to be below the defect.

2. Side of the triangle closest to nose should be vertical.

3. Outline of the flap ought to rise in a curve toward the tail of the eyebrow and extend down for several cms. toward the ear lobule.

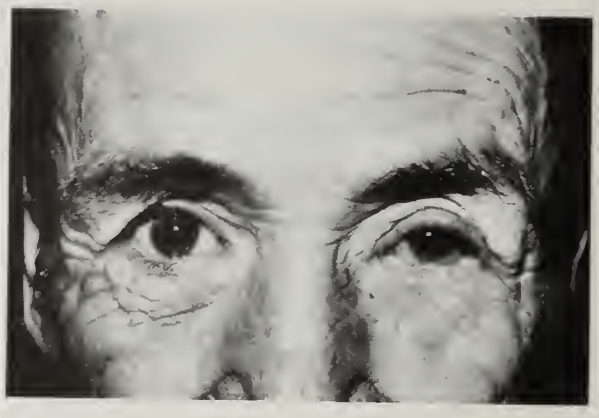


Figure 16: *Basal cell carcinoma involving entire margin of left lower lid.*

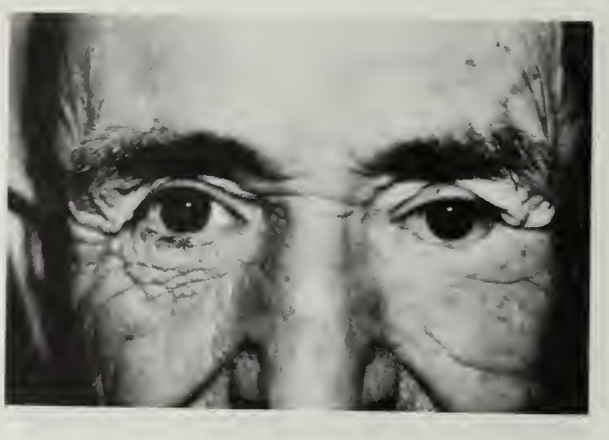


Figure 17: *Appearance two years after excision of tumor involving entire margin of left lower lid and reconstruction with Mustardé rotating cheek flap.*

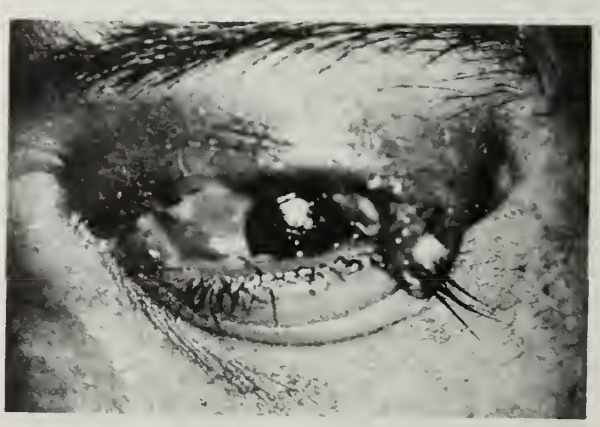


Figure 18: *Necrotizing reaction to bee sting with loss of entire margin of left upper lid.*



Figure 19: *Appearance of left upper lid 8 months after correcting lid margin with a Cutler-Beard flap. Patient is using false eye-lashes.*

4. Flap must be adequately undermined from the lowest point of the incision in front of the ear, across the entire cheek to one cm. below the apex of the excised triangle.

5. The deep tissues of the flap should be fastened to the orbital rim at the outer canthus, to prevent the weight of the flap from pulling the lid.

The Cutler-Beard full thickness flap of the lower lid is brought upwards under a 3 or 4 mm. wide marginal hammock or bridge of the lower lid and sutured into position, in two layers, to fill the defect in the upper lid.. After two months the new upper lid margin is created by dividing the flap and suturing the skin to the conjunctiva with interrupted silk suture. More extensive details can be obtained from a textbook of Ophthalmic Plastic Surgery (7). Some surgeons use the same technic of vertical sliding flap from the upper lid to correct a defect involving the margin of the lower lid. However, for the lower lid I prefer, as I have outlined, the use of the horizontal sliding flap for replacement of up to 80 percent of the lower lid. The Mustardé rotating cheek flap seems desirable when the defect in the margin exceeds 80 percent of the original lid length.

Summary

There are many different ways of performing reconstruction of lids. The author has presented a scheme of the technics found useful and successful in management of lid repairs. Lesions involving only the skin can be excised and followed by border to border suturing the defect or by filling the gap with a horizontal sliding skin flap. When the lesions are found in the margin of the lid, the repair procedures may select one of several technics, depending upon site and size of the lid defect.

Resumen

Existen numerosas maneras de reconstruir los párpados. El autor ha presentado un esquema de aquellas técnicas para el manejo de la reparación de los párpados que han probado ser útiles y exitosas. Lesiones que solamente envuelven la piel pueden ser removidas y corregirse el defecto por aproximación de borde a borde o llenando el defecto con un colgajo horizontal de piel deslizante. Cuando las lesiones se encuentran en el margen del párpado se puede seleccionar una de varias técnicas dependiendo del lugar y el tamaño del defecto en el párpado.

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REIMPLANTATION OF NEARLY AMPUTATED UPPER LIMB: A CASE REPORT

David Rodríguez Pérez, MD

The severance of all soft tissue structures of an extremity should not be an obligatory indication to complete amputation. All efforts should be made and measures taken to reanastomose nerves and blood vessels, and if necessary, substitute portions of missing artery and vein in order to try salvage (1). In this paper we present and discuss one such case.

Case Report

A 29 year old white male veteran was referred on August 23, 1973 from another hospital in the middle of the night with a right arm tourniquet, after undergoing suturing of bleeding arteries and veins for completion of amputation of right arm. One hour prior to admission, the patient had broken a window pane with right fist and his right arm was entangled in the broken glass avulsing all tissues in the antecubital fossa, leaving only a 1 1/2" bridge of skin posteriorly at the level of the olecranon. The distal arm was cold, cyanotic and no pulses were palpable. Under brachial block anesthesia the tourniquet was removed and inspection of the wound revealed:

1) 12 cm gap in the brachial artery.
2) 3 cm gap in the median nerve and the missing segment hanging among the ragged muscle fibers.
3) Transected radial nerve.
4) Partially transected ulnar nerve.
5) All veins had been either ligated or were thrombosed.
6) All musculature was cut through, or raveled down to the humerus or elbow joint.
7) Only 1 1/2" skin bridge posteriorly left intact.

Operation:

The left groin was prepared and under xylocaine 1 percent a 12 cm segment of left saphenous vein was resected and filled with diluted heparin. Then the attention was directed to the arm. Arterial ends were trimmed after removing the ligatures and vascular clamps were applied to proximal artery. Forearm was compressed until thrombi from distal arteries were expressed out and liquid blood came out. Diluted heparin was then instilled into distal arteries.

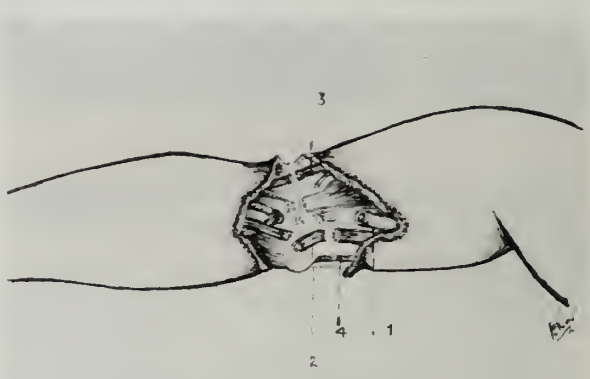


Figure 1: *Schematic representation of avulsed right arm structures: 1) proximal, brachial artery; 2) free segment of median nerve found in between the tissues: 3) totally transected radial nerve; 4) partially transected ulnar nerve.*

The free portion of the median nerve was used as a bridge and anastosomed with interrupted stitches of 6-0 Ethyflex to proximal and distal segments. Radial and ulnar nerves were equally treated after suitable mobilization.

The free vein graft was reversely anastosomed to both ends of the brachial artery with Ethyflex 5-0 using Carrel's technique. On releasing the vascular clamps there was abundant oozing from the cut muscle surface. Only few non-anatomical approximating "en masse" stitches were taken leaving wound edges wide open. An elastic bandage was firmly applied and the arm placed in a right angle metal splint and elevated over patient's breast. Operation started at 2 AM and finished 6 AM. The fingers regained color and digital pulses were palpable but the arm became tremendously swollen.

Post-operatively, the patient received blood transfusions and antibiotics. On the 7th post operative day the dressings were changed. The open wound appeared healthy and, al-

From the Veterans Administration Hospital, San Juan, P. R.

though the arm was swollen, both radial and ulnar pulses were palpable. The distal arm was anesthetic, and fingers and wrist were immobile and paralyzed.

Patient was started on passive exercises and was discharged on September 18th to continue physiotherapy and electrical stimulation as out-patient.

On February 1974 patient could move all fingers. On March 3rd, 1974 patient was discharged from physiotherapy. Patient was able to use his arm, hand and fingers normally and started breeding rabbits for commercial purposes.

In view of the good results a subclavian arteriogram was done (Figs. 2, 3).



Figure 2: *Axillary arteriogram. Arrows indicating the bridging reverse saphenous vein.*



Figure 3: *Venous phase of axillary arteriogram fails to show the cephalic nor basilic veins, instead a rete venosus developed between arm and forearm.*



Figure 4: *Hand showing complete radial nerve regeneration.*



Figure 5: *Hand showing median and ulnar nerves regeneration.*

Comments

Kleinert, Kasdan and Romero (2) while performing a replantation recommend gentle handling of blood vessels and flushing the clots with heparin. They give great importance to a patent distal outflow tract and late neurolysis.

Malt and McKahnn (3), in an article which I consider fundamental, agree with the previous authors, but in one of their reported cases they had difficul-



Figure 6: *Excellent extension of arm.*



Figure 7: *Flexion and fist making showing still slight debility of trigger mechanism.*

Figures 4, 5, 6 and 7 show results after surgery.

ties with the neuromas found in late neurolysis.

In the total amputated limb it is important to anastomose at least one vein, but if there is continuity of bone or a small bridge of skin, apparently these structures can take over the burden of the immediate congestion until new vessels and recanalization of veins occur in the immediate healing phase, as we observed in our case.

In these times of superspecialization it is difficult to handle a case like a replantation in the middle of the night. It is quite different during daytime when all facilities; blood bank, complete operating room personnel, neuro-surgery, orthopedic and plastic surgery consultants are readily available.

The training of residents in the gentle handling of tissues, performance of excellent vascular anastomosis, repair of tendons and muscles, and the mastering of pre and postoperative care should prepare them fit in attempting reimplantation of limbs.

Complications, which constitute the unpredictables of our science and art of surgery, may prolong hospital stay or may even require the amputation of the replanted limb in order to save the life of the patient.

Clinical investigation and animal experimental work as well as autopsy and pathological studies have constituted the fundamental stone in the continued progress of the different surgical endeavors.

The fear of complications and the fear of lawsuits have deterred surgeons in attempting more often reimplantation of limbs reducing this type of surgery to a few sporadically published cases.

Summary

A case of reimplantation of nearly amputated upper limb is presented in which bone continuity and a small posterior bridge of skin afforded an immediate blood outflow and no vein anastomosis was performed.

Saphenous vein was used to bridge a large arterial defect.

Nerves were primarily anastomosed and a free segment of median nerve was re-sutured followed by total regeneration.

A new rete venosus substituted the veins of the arm.

Arm and hand recovered totally all functions after a non anatomical "en masse" approximation of muscles and tendons.

Superspecialization and lawsuits pose an obstacle to the progress of this type of surgery.

Resumen

Se presenta un caso reimplantación casi total del brazo derecho en donde no se hizo anastomosis venosa, sirviendo un puente de piel y la continuidad osea de escape inmediato a la congestión venosa.

La vena safena izquierdaseusó como puente en el gran defecto arterial.

Los nervios se anastomosaron primariamente y un trozo libre de mediano se reunió a los extremos del mismo seguido de regeneración total.

Brazo y mano recuperaron todas sus funciones.

Un rete venoso substituyó las venas del brazo.

La superespecialización y las demandas legales ofrecen obstáculos al progreso de este tipo de cirugía.

Acknowledgment

For the interest and dedication to the rehabilitation of this patient, a word of recognition and gratefulness to the Physical Medicine and Rehabilitation Department of the Veterans Administration Hospital.

For the arteriographic studies, our thanks to Dr. E. Medina de la Baume from the Radiology Service of the Veterans Administration Hospital.

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EDITORIAL

REIMPLANTATION OF SEVERED EXTREMITIES

In an accompanying article in this issue of our Boletín, Dr. David Rodríguez Pérez reports a successful reimplantation of a partially severed arm. The surgical community is aware of the surgical achievements of Dr. David Rodríguez during his lifetime, and of his excellence as surgical operator and as humane physician, so it is not surprising to see this successful report, especially when placed in its proper perspective. Only in recent years has successful reimplantation of extremities been achieved with certain regularity and even so, long term results are still usually poor.

Several technical points mentioned by Dr. Rodríguez should be stressed. First, the warm ischemia time is crucial since survival will be inversely proportional to it. This is true of all organs and has been amply demonstrated in the past in many laboratories, including ours, for heart, kidney and liver. Muscle, skin and blood vessels partake of this same law, although tolerance to ischemia is higher than for solid organs.

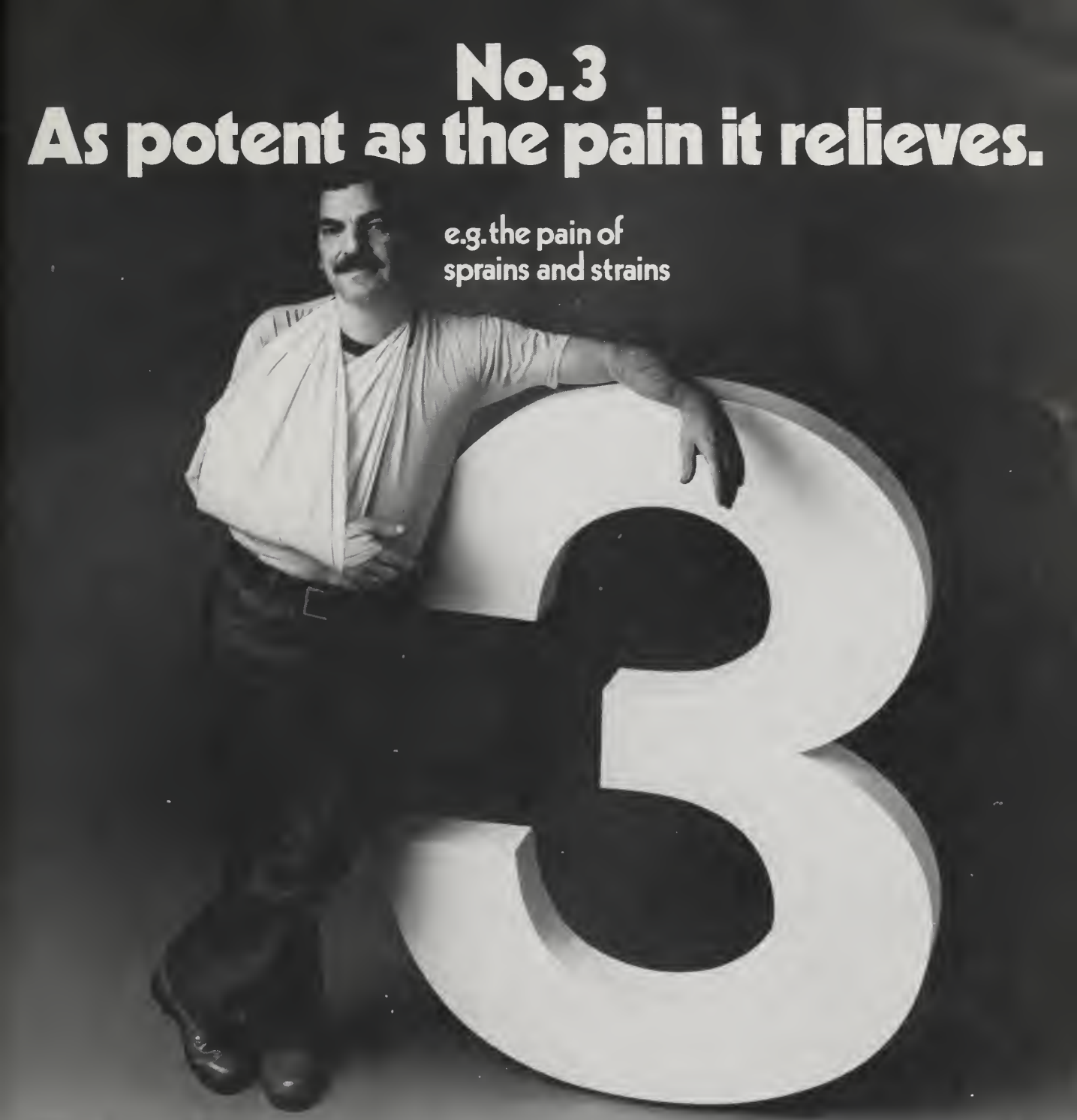
Second, the patency of the distal arterial tree must be immediately assessed and established. Manual compression of the distal extremity may be a good maneuver to express clots that by this time have usually formed. Immediate flushing with a cold heparinized solution is mandatory. Perhaps we should state here that the electrolyte composition of this solution is important in achieving survival. As a general rule, heparinized Ringer's Lactate is used in perfusion of severed extremities. It has been previously shown by several investigators that this may be detrimental to the endothelium of blood vessels as evidenced in scanning electron microscope studies. In our laboratory, we have shown that perfusion with solutions having an intracellular composition (high K^+, low Na^+) plus injection of certain steroids in pharmacological doses enhance extremity survival in dogs. We have recommended the use of this regime in clinical series. Solutions with similar composition have been used successfully in kidney and liver preservation.

Third, particular attention must be given to a meticulously delicate surgical technique. There is no way in the world that drugs or solutions can substitute the gentle handling of tissue, the performance of perfect vascular anastomoses, briskly bleeding healthy surfaces, and excellent pre and post operative care. Absolute aposition of nerve tissue is mandatory. As a rule the skin should be left open and in some cases longitudinal fasciotomies may be of value.

Salvage of severed extremities should be attempted in all cases of traumatic amputation. Attention to details of technique in surgery and perfusion, as well as an active, vigorous, post-operative physical therapy program may result in salvage of usable, functional extremities.

Eduardo A. Santiago-Delpín, MD

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N O T I C I A S

AMA NEWS RELEASE:

NEW FINDINGS REPORTED IN HEAT TREATMENT FOR CANCER:

CHICAGO– New research into the use of heat to treat cancer is reported in the May 17 issue of the Journal of the American Medical Association.

Heat treatment reduced or substantially eliminated cancer in 21 patients, say Harry H. LeVeen, M. D., and colleagues, of Veterans Administration Hospital and Downstate Medical Center of State University of New York, Brooklyn.

The heat was introduced by radiofrequency radiation. Cancerous tissue became considerably hotter than surrounding tissue, up to a temperature of 118 degrees, Dr. LeVeen reports.

The technique is based on the knowledge that blood flow through a tumor is very sluggish, less than 2 to 15 percent of flow through surrounding normal tissue. Blood flow cools tissue. Cancerous tissue cools much slower, thus allowing a high degree of heat to be directed into the tumor. The heat causes destruction of cancerous tissues, without destruction of normal tissues.

The blood flow through body tissue acts like a radiator, with greater cooling occurring when the flow is rapid, Dr. LeVeen explains.

The 21 patients had a variety of different types of cancer. Some were lung cancer, others cancers of the intestines and some of the head and neck. Treatment was with a radiofrequency generator constructed specifically for the treatment process.

In an accompanying editorial in the same issue of the Journal, Joan M. Bull, M. D., and Paul B. Chretien, M. D., of the National Cancer Institute at Bethesda, Md., trace earlier studies in use of heat to treat cancer, and declare that the results of the LeVeen studies may allow a more widespread use of this method than of those developed by earlier researchers. Drs. Bull and Chretien call for more human trials under very careful controls.

More carefully designed and controlled studies are now needed to investigate the potential of heat to increase the tumor-kill achieved with radiotherapy and chemotherapy, in view of increasing evidence of the superiority of multitypes of therapy in cancer treatment, they say.

Future clinical trials must be designed with precise attention to details of temperature measurement in the tumor and normal tissues and the determination of the effects on all vital functions, they say.

NEW DRUG HELPS CONTROL EPILEPTIC SEIZURES

CHICAOO– An important new drug to help control certain types of epileptic seizures is now available in America. It is clonazepam.

Researchers at Harvard Medical School and at a medical center in Denmark report in two separate articles in the May issue of Archives of Neurology, a scientific journal of the American Medical Association, that clonazepam has proved effective in controlling seizures in some children who had not been helped by earlier drugs.

Thomas R. Browne, M. D., Harvard neurologist, reports that clonazepam has proved effective in coping with five types of epileptic seizures. It is rapidly absorbed by the body and passes quickly from the blood to the brain, says Dr. Browne.

The drug sometimes has side effects of drowsiness and behavior changes, which subside with regular use, and may be minimized by lower doses.

FROM FDA DRUG BULLETIN

METRONIDAZOLE (FALGYL) BOX WARNING

Labeling for metronidazole has recently been revised to include a box warning of carcinogenicity in rodents and to reduce the recommended duration of treatment for trichomoniasis. In addition, metronidazole vaginal inserts will no longer be marketed because data supporting their effectiveness are inadequate.

Evidence developed over the last five years has shown that metronidazole (Flagyl) is carcinogenic in certain mouse species and possibly in rats as well. Studies with the drug in hamsters have not revealed an increased tumor incidence. The positive rodent studies involved chronic (lifetime or almost lifetime) oral administration and included one study in which intermittent (every fourth week) administration was used. It is not possible to extrapolate these data directly to humans, but, as with any animal carcinogen, metronidazole must be considered a potential human carcinogen. Because the dose of drug used in the animal studies was higher than the human dose and because

the duration of treatment was far longer than human treatment, both absolutely and in comparison with the life span of the two species, FDA believes the risk of human carcinogenesis is low.

Nevertheless, every effort should be made to limit use of the drug to those in whom it is clearly indicated and to prescribe the lowest effective dose. The present labeling revision recommends a treatment regimen for trichomoniasis of 250 mg three times daily for seven days for both males and females. Other regimens involving smaller total dosages have been reported in the medical literature, but FDA believes that their effectiveness is not yet fully established. Additional studies of such regimens are ongoing at present.

NEWS FROM THE AMERICAN COLLEGE OF SURGEONS

CHICAGO, ILLINOIS – The American College of Surgeons and the American Board of Surgery have agreed to correlate the College's Surgical Education and Self-Assessment Program (SESAP) with the Board's recertification process. The first voluntary recertification examination is to be offered in the Fall of 1980. The American Board of Surgery will inform candidates for recertification they should be familiar with the body of knowledge covered by SESAP. The agreement in essence emphasizes that the part played by the College is education, and that of the Board is determination of knowledge as well as of other indications of competence.

The agreement between the American College of Surgeons and the American Board of Surgery indicates that the clinical and other problems addressed by SESAP, as well as other educational activities of the American College of Surgeons, will constitute the basis for questions in the examination portion ot the Board's mechanism for voluntary recertification.

SESAP is a voluntary, confidential, continuing education program for surgeons and others interested in surgical science and practice. Enrollees participate in the program to any degree they choose, and at any time or place. No grading such as pass-fail is given, nor is there any record of the level of performance of any individual.

SESAP is offered in the form of three self-assessment books containing 750 items covering nine areas of surgical knowledge. A 500-age Syllabus duplicating the items and containing the critique of each of them, together with references and a comprehensive Index, is part of the SESAP package.

The body of knowledge covered by SESAP is that with which all surgeons, regardless of specialty, should be familiar. All surgical specialties were represented on the ten committees that constructed SESAP.

SESAP was first offered in 1971. Since then, a total of more than 29,000 individuals have enrolled in SESAP, SESAP II, which was released in 1974, continues to enroll individuals at a steady rate. SESAP III, the third program, will be available in the fall of 1979.

Complete information about SESAP and applications for enrollment in SESAP II are available from: SESAP, c/o American College of Surgeons, 55 East Erie Street, Chicago, Illinois 60611.

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NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method *(Federal Register 37:* 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

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Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or

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Precautions: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

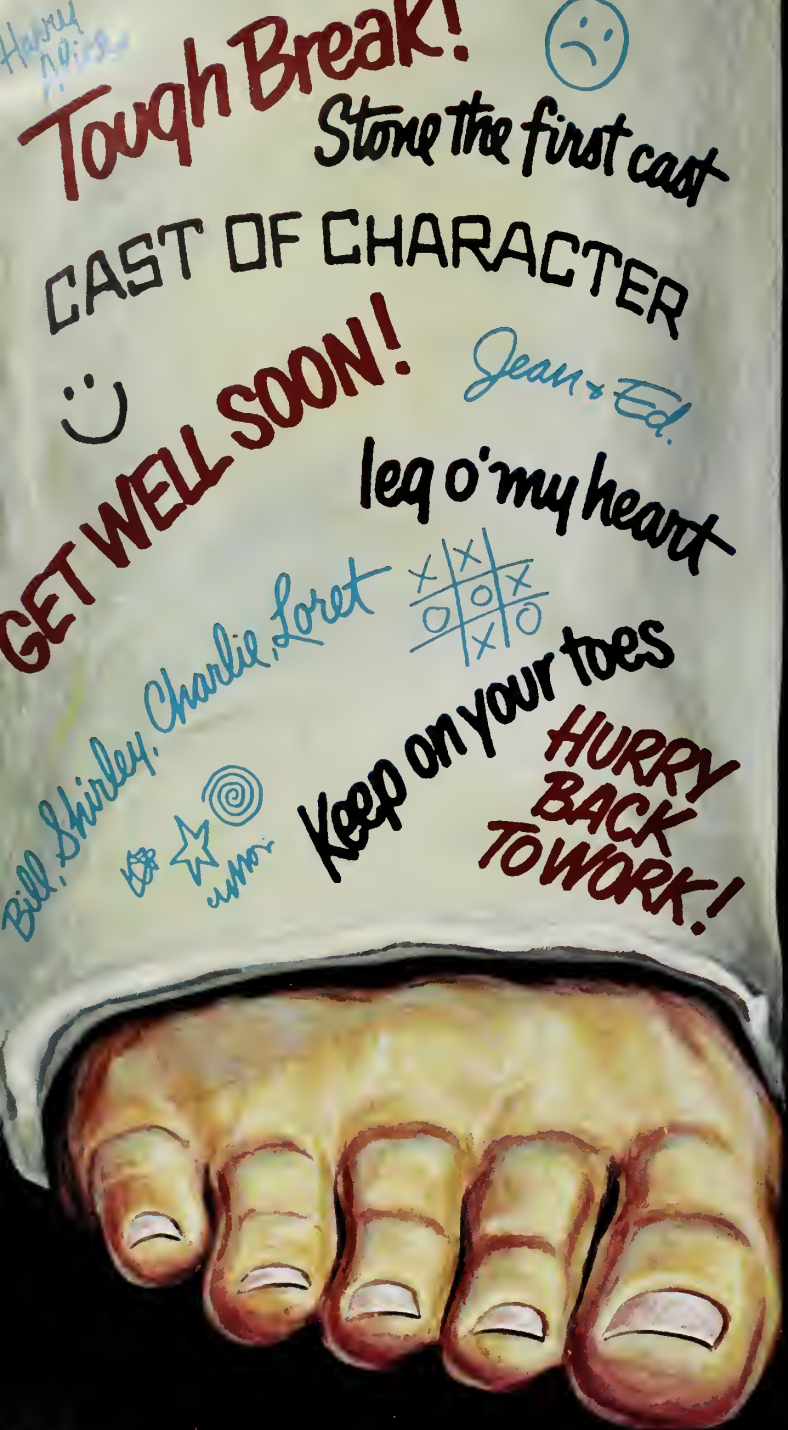
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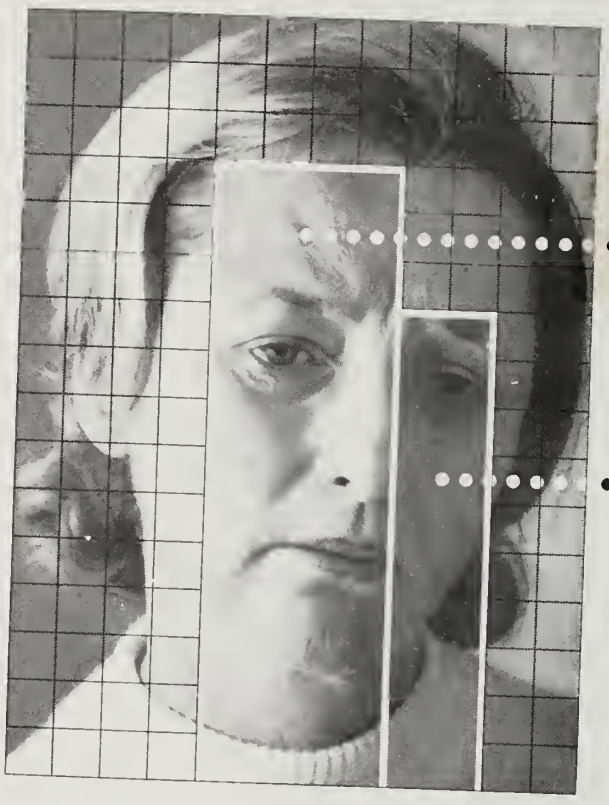
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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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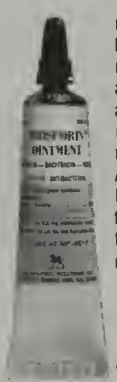
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Volumen 68 Octubre 1976 Número 10

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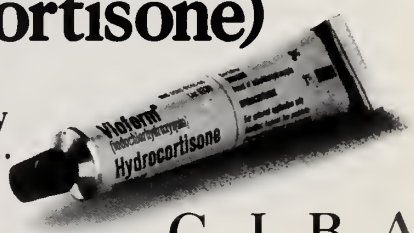
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PROCIDENTIA UTERI AND ITS MYTHICAL PROTECTION AGAINST CERVICAL CANCER HISTORICAL REVIEW

Enrique Pantoja, MD
Robert W. Axtmayer, MD
Ismael Rodríguez Ibañez, MD

The earliest observations regarding procidentia uteri are traceable to the writings of the Father of Medicine himself (1). There can be little doubt that he was referring to this condition when he wrote about the uterus hanging down between the patient's legs like a scrotum (*). The condition is also mentioned by many of the ancient writers who followed, from Celsus, Soranus (2), and Aretaeus (3), to Aetius, Paulus (4), and Haly ben Abbas.

Some of these writers seemed to be familiar with total prolapse associated with uterine inversion as a result of a difficult labor, abortion or trauma, and they considered this type of prolapse to be fatal (3). Uncomplicated procidentia seemed to be less well known, and was regarded as a very rare affliction.

According to Morgagni (5), Fernelius gave a good account of uterine displacements, and designated as descent the partial downward displacement, and as prolapsus the total expulsion of the uterus associated with inversion. The account would have been completed, says Morgagni, if he had not failed to mention total prolapse without associated uterine inversion (procidentia). The omission is amended in Morgagni's own account, however, neither he nor his teacher, Valsalva, had any personal experience with these disorders. Here the founder of pathologic anatomy admits of having heard of one case of prolapse associated with inversion in his own country, but without inversion, not even once! His knowledge of the disease came mainly from the ancient writers.

For almost a century following the work of Morgagni, French gynecologists debated among themselves regarding the existence of "chute" or "précipitation" (procidentia) (6, 7). It was argued by some, as late as 1858 (7) that this was nothing but a hypertrophy of the cervix, the uterus remaining in its normal position.

In the meantime, John Clarke (8), a former student of the Hunter brothers, called attention to a lesion of the cervix which he called cauliflower excrescence, later to be recognized as cervical carcinoma. But the recognition of this lesion as a separate entity, and especially, its association with procidentia uteri was to come by very slowly.

Many recent authors have been puzzled by the apparent rarity of the association of these two conditions, despite the fact that neither one is by itself rare. Sholes (9) attributes to Weinlecher (1862) the first report in the literature on uterine cancer and prolapse, but he gives no reference. Duparque (10), however, cites an earlier case published in 1820 (11), and he himself reports the clinical history and postmortem findings on a woman who had a uterine prolapse for 45 years and whose uterus was found to be the site of cancer at autopsy. Yet, towards the end of last century there were still so few cases on record that in 1880 Fritsch spoke of an apparent immunity against cancer in the prolapsed uterus (12).

Fifty years later Delveaux (13), struck by the paucity of reports on the subject, addressed a questionnaire to the outstanding German and French gynecologists of the day regarding the coexistence of these two entities. Most of the authorities questioned had never seen the two associated, and Delveaux was also convinced that the rarity of the association represented a form of immunity.

During the last three decades the number of cases

** · Some authorities, notably Francis Adams, do not recognize this part of the Hippocratic collection as being genuine, but as being written perhaps by one of his disciples.*

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of carcinoma of the cervix associated with procidentia has increased to the point where not only do many authors question the rarity of the association, but some (14) have even come to the conclusion that in elderly patients the incidence of carcinoma of the cervix is higher in the prolapsed uterus than in the normally situated organ. One of the explanations for the supposed rarity of the association has been the fact that procidentia generally occurs at an age when carcinoma of the cervix is no longer common (15, 16).

But age is not the only factor contributing to the rarity myth. Cervical carcinoma in the completely prolapsed uterus may have an inocuous, misleadingly innocent appearance (16, 17), and it may be mistaken for the common decubitus ulcer so frequently seen in this condition (Fig. 1). Many of these carcinomas have been missed on pelvic examination by competent gynecologists (17), and it has been recommended that biopsies be performed more freely in this condition in an attempt to detect early carcinomatous change (18). In some cases the cervical lesion has presented as a pathological surprise in uterine specimens removed for procidentia (19). It seems likely that many incipient cases of this association have been missed in the past.

Carcinoma of the cervix associated with procidentia is also a milder disease (18), than the average cervical cancer (and may be age plays a role in this too), so that a patient may live with the carcinoma for a number of years and die of unrelated causes without the malignancy ever being discovered. This was more likely to occur in the days when the rarity myth was developing.

When cancer was a clinical diagnosis pain was considered an essential symptom of the disease, the 'sine qua non' which distinguished it from the painless scirrhus. Pain is rarely associated with carcinoma in the prolapsed uterus; thus, the early nineteenth century physician would not have ventured a diagnosis of cancer in the absence of this symptom. Furthermore, the physician in those days was not wont to meedling with the genital organs of his female patients, which must have contributed to the paucity of observations regarding cancer in procidentia uteri.

The lack of familiarity with the prolapsed uterus (and with the entire female sexual anatomy for that matter) may be appreciated from the directions given by Sir Charles Mansfield Clarke, member of the Royal College of Surgeons and Surgeon to the Queen's Lying In Hospital, to his physician readers. In his book on diseases of women, published in 1824 (20), he advises them: "The difference between this disease (procidentia) and the male sexual organ is too obvious to be mistaken by anyone who will pay attention to it". And, as if to clear up any lingering doubt, he goes on to add: "The long diameter of the opening of the urethra in the latter is from before to behind, whereas that of the os uteri in females is from side to side, and this alone is enough to make the difference".

The modern physician is aware of the possibility of malignancy associated with prolapsed uteri, which is perhaps why the reported incidence of the association has been increasing (17). However, carcinoma



Fig. 1A - *Procidentia with decubitus type ulceration. No malignancy found.*



Fig. 1B - *Same patient two weeks after removal of two large ovarian cysts (one of which was lodged in the pelvis) and uterine suspension. Ulceration is healing.*



Fig. 2: *Reducible procidentia with a carcinoma of the cervix.*



Fig. 3: *Large uterus with long standing, irreducible procidentia and a cervical carcinoma.*

tends to occur in procidentia of long standing (ten years or more) (14), and women who are still willing to tolerate this condition for so long are not likely to be much concerned with a painless induration in the prolapsed organ. Unlike the younger woman seeking early attention for postcoital bleeding, the elderly female with a carcinoma associated with procidentia is more likely to neglect her disease (Figs. 2 and 3), and thus still contribute to the seemingly low incidence of the association.

There is still another factor which may affect this incidence, and that is race. Black women are not as commonly affected by procidentia as are Caucasians (21). This has been attributed to a higher incidence of pelvic inflammatory disease resulting in fibrosis and adhesions between the pelvic viscera, to a better muscle tone, and to a greater frequency of contracted pelvis among the black women (21). On the other hand, these same women seem to be preferentially affected by carcinoma of the cervix.

Pathological Findings

Carcinoma associated with procidentia is usually of the epidermoid type, invasive, and arises from the uterine cervix. However, in situ lesions are occasionally found (17, 22), and adenocarcinoma of the cylindroma type has been reported (22). The malignancy may also occur in the vagina (23) (Fig. 4), and double lesions involving both the cervix and the vagina have been reported (24). Adenocarcinoma of the endometrium may occur in prolapsed uteri (25, 26), and in view of the concordance in age incidence of both conditions, this association should not be rare. However, to judge from the number of reported cases (27), it has generated less interest than the cervical lesion.

Cervical cancer in procidentia has been found to be slow in spreading, a phenomenon which has been attributed to impaired lymph and/or venous drainage (15). Regional involvement of the pelvic organs may occur

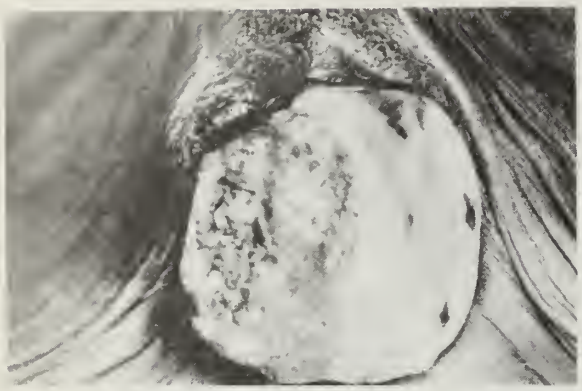


Fig. 4: *Ulcerated carcinoma of the right lateral fornix in a colored patient with procidentia. There are pigmented patches in the uninvolved mucosa around the cervical os.*

late in the course of the disease. Distant metastases are rare, but have been reported (28). Percival (29) divided cervical cancer with procidentia into two groups: (1) the slow growing, mature form, in a cornified cervix prolapsed for years, and (2) the rapidly growing, anaplastic tumor in the recently prolapsed uterus of a young woman. Most cases seem to belong to the first group.

Treatment

This has been mostly surgical and has varied from a simple vaginal hysterectomy to a pelvic exenteration (28, 30). Because of the slow growth of these tumors and the low incidence of metastases, a vaginal hysterectomy often succeeds in controlling the lesion. When the extent of the disease requires a more radical procedure the results of surgery alone are not good (29).

Radiotherapy has been successfully used as the sole modality of treatment (31, 32) as well as in combination with surgery (preoperative radiation) (33, (34). When the procidentia is reducible (Fig. 2), the usual intracavitary radium insertions for carcinoma of the cervix may be performed. When the procidentia is of long standing and irreducible (Fig. 3), intracavitary radium, but not the colpostats, may still be applied. In either case the intracavitary therapy may be combined with external irradiation. Occasionally, radiotherapy not only succeeds in controlling the tumor, but the induced fibrosis and retraction may result in spontaneous correction of the procidentia (32, 35). A course of external irradiation with or without intrauterine radium therapy may be followed by a simple hysterectomy and the results of this combination have been satisfactory in most cases.

Summary

Cervical cancer and procidentia uteri are both relatively common disorders, yet this association in the same patient has been considered rare, probably because (1) their peak incidence occurs at different ages, (2) they differ in racial predisposition, (3) the elderly patient with long standing procidentia is likely to overlook a superimposed malignancy, and (4) cervical carcinoma in procidentia is often slow growing, causes the patient few additional symptoms, and may be confused with the decubitus ulcerations commonly associated with procidentia, so that the physician himself may miss the tumor.

In this review the historical evolution of the mythical immunity of the prolapsed uterus to cancer has been traced to still another factor, a general ignorance on the part of the physician regarding diseases of the female sexual organs, particularly cancer, until the mid nineteenth century.

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SINDROME DE ANGELMAN O DE LA MARIONETA ALEGRE

A. Pérez Comas, MD, PhD

Angelman en 1965 informó de tres pacientes que presentaban características faciales peculiares, deambulación parecida al movimiento de las marionetas y paroxismos de risa. Denominó la condición "niños marionetas". Bower y Jeavon, en 1967, informan de otros dos niños afectos de la misma condición, nominándola "síndrome de la marioneta alegre" ("Happy Puppet Syndrome") (2). Hasta el presente se han descrito un total de catorce pacientes afectos de la condición, diez en Inglaterra, uno en Canadá, uno en los Estados Unidos de Norteamérica y dos en Israel (1-7).

En los últimos dos años hemos venido siguiendo a un niño de origen español, afecto de esta condición, el cual motiva esta comunicación.

Informe del Caso

L. A. P. V. nació a término de una madre de 24 años de edad y un padre no consanguíneo de 23 años de edad. El embarazo estuvo complicado con una infección respiratoria severa a los 2 meses de embarazo, hiperémesis gravídica en el primer trimestre y flujo vaginal abundante, especialmente en el octavo mes. Desconocemos los medicamentos dados a la madre en España. El niño nació en el Hospital Municipal de Lugo, el 2 de junio de 1970 en Galicia. siendo atendido por una comadrona. Hubo rotura precoz de membranas 20 horas antes del parto. Nació cianótico, presentando un peso de 3500 gramos y una longitud de 50 centímetros.

A los dos años y 10 meses de edad, nos fue referido a la Clínica de Problemas Genéticos para evaluación diagnóstica, debido a microcefalia (notada desde el mes y medio de edad), retardo psicomotor severo (sólo se volteaba), facies inexpresiva peculiar con sonrisa y protusión frecuente de la lengua. Su evaluación mostró los datos somatométricos detallados en la Tabla I, al igual que se observó (figuras 1-2): occipucio aplanado, cejas espaciadas, surco nasolabial prominente, filtro alargado, boca grande, labio inferior prominente, dientes algo irregulares y amarillos, ligero estrabismo convergente, ojos marrón claro y pelo marrón claro, protrusión de la mandíbula, cuello corto, tórax asimétrico, en quilla, cifosis, dedos II-V de las manos en flexión, pié equinovaro bilateral y reflejos hiperactivos.

La prueba de desarrollo de Denver a los 29 meses de edad reveló un retraso marcado en todas las áreas, funcionando por debajo de un nivel de 7 meses de edad. La prueba de desarrollo Gessell reveló una edad basal por debajo de los tres meses, un nivel de ejecución normal de 2.91 meses, un nivel de ejecución funcional de 4.16 meses, y un nivel de ejecución máxima de seis meses.

A los 9 meses y a los 16 meses de edad le fueron realizados estudios electroencefalográficos en España, los cuales mostraron irritabilidad centraencefálica cortical difusa, no observándose signos focales ni asimetría interhemisférica.

Estudios cromosómicos y aminoácidos plasmáticos realizados en nuestro laboratorio mostraron un patrón normal.

Los dermatoglifos revelan un ángulo atd derecho de 38^{o}, izquierdo de 49^{o}, un bucle distal en espacio interdigital IV de ambas palmas, surcos y líneas abundantes en las palmas y plantas, campo abierto en ambas áreas halucales y los siguientes patrones digitales: mano derecha - dedo 1: espiral, 2: bucle radial 3: bucle radial 4: bucle cubital 5: espiral. Mano izquierda - Dedos 1-5: bucles cubitales.

El primer diente le salió a los 6 meses de edad. A los 34 meses tenía ocho superiores y 8 inferiores. Se volteó a los 32 meses; a los 55 meses se sentó y a los 58 comenzó a pararse y caminar con soporte. La deambulación es irregular y semeja los movimientos bruscos de una marioneta. A los 5 años aún no habla.

Posterior a su nacimiento su madre tuvo un aborto espontáneo de dos meses de causa desconocida, y una niña que actualmente tiene un año y es completamente normal. Esta niña es hermana de madre solamente.

Al presente el niño se encuentra bajo tratamiento ortopédico y de fisioterapia.

Discusión

La enfermedad caracterizada por Angelman en 1965 (1), ha sido informada en un total de 15 pacientes, incluyendo el nuestro. Todos los sujetos afectos presentan la facies característica, retardación mental y ausencia del

De la Sección de Endocrinología Pediátrica y Genética Médica del Hospital Dr. R. E. Betances, del Centro Médico de Mayagüez.





Figuras 1-2: L. A. P. a los 34 meses de edad.

TABLA I
MEDIDAS DE L.A.P.V. A LOS 34 MESES DE EDAD

Peso	10 kilos	circ. torácica	56 cms.
Estatura	92 cms.	abdomen	45 cms.
envergadura	85 cms.	canto externo	11 cms.
S.S./S.I..	1.25	canto interno	2 cms.
Circ. craneana	45 cms.	Distancia interpupilar	5.5 cms.

habla. Estos y otros hallazgos están detallados en las Tablas II y III.

La facies típica se caracteriza por una cara poco expresiva con sonrisa frecuente, lengua y mandíbula protuberante, occipucio aplanado y microcefalia. Nosotros hemos observado que los casos informados también presentan cejas algo espaciadas, hipertelorismo, surco nasolabial marcado y filtro alargado. Asociados a esta facies se observan paroxismos de risa, ataxia y deambulación con movimientos similares a los de una marioneta, anomalías electroencefalográficas, convulsiones, hipotonía y retardo motor, anomalías dentales con dientes

TABLA II
HALLAZGOS MAS FRECUENTES EN LOS PACIENTES AFECTOS DEL SINDROME DE LA MARIONETA ALEGRE

	Angelman			Bower & Jeavons		Berg & Pakula	Mayo y Colabs.			Moore & Jeavons		Mussey & Humpton	Elian		Pérez Comas
Signos y Síntomas	1	2	3	1	2	1	1	2	3	1	2	1	1	2	1
Facies típica	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ataxia	+	+	+	+	+	+	–	–	–	+	+	+	+	+	+
Risa paroxística	+	+	+	+	+	+	+	–	–	+	–	+	+	+	+
Retardación Mental	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Epilepsia	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–
Anomalías EEG	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Ausencia del habla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hipotonía	+	+	+	+	+	+	–	+	–	+	+	–	+	+	–
Anomalías múltiples *	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

** - Otras anomalías detalladas en Tabla III.*

TABLA III
ANOMALIAS MULTIPLES ADICIONALES EN LOS 15 PACIENTES CONOCIDOS

Anomalía Congénita	Número de Pacientes
Depresión occipital	13
Microcefalia	12
Protrusión de la lengua	13
Protrusión de la mandíbula	12
Anomalía de labios o dientes	7
Ojos azules (pelo claro)	13
Anomalías oculares	13
Pigmentación escasa	9
Atrofia óptica	4
Estrabismo	3
Movimientos anormales	1
Catarata congénita	1

de forma y disposición irregular, orejas de inserción baja, redundancia en el cuello, abducción del quinto dedo, y un surco horizontal occipital. Las anomalías oculares incluyen pigmentación defectuosa, atrofia óptica, estrabismo, movimientos anormales y cataratas congénitas (1-7). Muchos de estos pacientes presentan ojos claros y pelo claro. Todos los sujetos con ojos azules eran ingleses a excepción de uno israelí. Probablemente esto sea debido más a factores étnicos que de la condición. A pesar de ello 13 de los 15 pacientes

presentan una piel extremadamente blanca, poco pigmentada, lo que establece la duda si es una característica más de la enfermedad.

La etiología de la condición es desconocida. Todos los casos informados han sido esporádicos no observándose ninguna relación familiar. Los estudios cromosomicos realizados en 13 pacientes y los estudios de aminoácidos en 6 de los pacientes han sido normales. Al presente no existen datos necrológicos, ya que todos los sujetos están vivos.

Resumen

El síndrome de la marioneta alegre se caracteriza por una facies característica inexpresiva salvo por sonrisa, lengua protuberante, crisis paroxística de risa, retardación mental, microcefalia, ataxia y deambulación con movimientos similares a una marioneta, y otras anomalías asociadas. Es una condición rara de la cual se han informado 15 pacientes en la literatura, desconociéndose su etiología. Esta comunicación describe un sujeto varón evaluado en nuestra Isla.

Summary

Angelman's "Happy Puppet" syndrome has been reported in 15 different patients from England, Canada, U.S.A., Israel and the subject of this report who presents Spanish ancestry. The syndrome is mainly characterized by a characteristic expressionless facies, save for frequent smiling and tongue protrussion, mental retardation, ataxia, absent speech, paroxysm of laughter, microcephaly and other associated anomalies. The etiology of the condition is unknown.

Agradecimiento

Agradecemos al Dr. Roque Montalvo la ayuda prestada en la evaluación inicial del paciente, al Departamento de Fotografía del Centro Médico de Mayagüez las preparaciones fotográficas y a la Sra. Mirna Nazario por la excelente labor secretarial. Agradecemos a la Sra. Madeline Ruiz de Martínez la evaluación de Denver y a la Srta. Elsie M. Astacio, la evaluación motora de Gesell.

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CARCINOMA DEL ESTOMAGO CON EXTENSION A LA CABEZA DEL PANCREAS

Con Una Nota sobre la Técnica de Resección

Gerhart Ramírez Schon, MD
Juan R. Díaz Troche, MD

Con frecuencia el carcinoma del estómago envuelve la cola del pancreas por extensión directa, al igual que el colon o el hígado. En la mayoría de estos casos el cáncer está marcadamente avanzado, imposibilitando una resección radical curativa. En una fracción pequeña de los pacientes el carcinoma del estómago se origina en el píloro. De aquí se extiende a la cabeza del pancreas y al duodeno en todos los casos, en contradistinción a los carcinomas con origen en el antro cuya extensión microscópica al duodeno ocurre en solo 43 por ciento (5). Debido a su localización el cáncer pilórico produce obstrucción de la salida del estómago en una etapa temprana y por lo tanto presentan de un tamaño adecuado para intentar una resección curativa. Obviamente, la resección radical de estómago que se usa para el cáncer de estómago no se puede aplicar a una lesión en esta localización y con esta extensión. Solo es posible resecarla con una pancreatico duodenectomía.

Casos

Caso Núm. 1:

N.O.R., C.M.M. 19-91-42

Mujer de 69 años con dos meses de historial de debilidad, palidez, anorexia, mareos, fatiga y vómitos, sin pérdida de peso. Al examen físico presentaba una palidez marcada con presión arterial de 160/100 y pulso de 96/min. regular. No había nódulos palpables en el cuello, se encontraban sibilancias inspiratorias en ambos pulmones, se sentía una llenura en el cuadrante superior derecho del abdomen. No había masa en el abdomen, el hígado no se palpaba y el examen rectal y pélvico no demostraba masas anormales. Por laboratorio se encontró una anemia de 6 Gm. de hemoglobina, una fosfatasa alcalina normal y sangre oculta en la excreta. La placa de pecho no presentaba patología y el estudio del estómago con medio de contraste demostró una obstrucción parcial a la salida del estómago con un defecto de llenado en esta región. Se confirmó el diagnóstico de carcinoma de estómago por gastroscopía.

El 25 de junio de 1976 se intervino quirúrgicamente encontrando un tumor de 8 x 4 centímetros originando en el píloro con extensión al duodeno y la cabeza del pancreas. No había metástasis a hígado, peritoneo, cul - de - sac, ligamento redondo, omento, o ascites. La porta se separaba fácilmente de la masa tumoral al disecar el tunel intrapancreático. Se hizo una pancreatico-duodenectomía, omentectomía y hemigastrectomía. Se reconstruyó la continuidad del intestino con una anastomosis término-terminal de pancreas y jejuno y anastomosis término-laterales entre jejuno y colédoco inicialmente y el estómago después. La pérdida de sangre durante el procedimiento fue de 1,000 cc. La paciente se dio de alta al séptimo día post-operatorio sin complicaciones mayores y actualmente recibe quimioterapia en clínicas externas.

M. S. B., C.M.M. 09-84-79

Mujer de 69 años de edad con historial de aproximadamente un año de dolor epigástrico al comer con pérdida de peso de 38 libras. Al examen físico no se encontraron masas en el cuello y los pulmones estaban claros. Se encontraba una masa palpable en el cuadrante superior derecho del abdomen, pero no se palpaba el hígado y no presentaba masas en el ombligo o al examen rectal. El laboratorio reveló una anemia de 7.3 Gm. por ciento de hemoglobina, una fosfatasa alcalina normal y una albúmina de 3.4Gm. por ciento. La placa de pecho no demostró patología y las placas de estómago con medio de contraste demostraron una obstrucción a la salida del estómago. El 13 de septiembre de 1976 se operó la paciente y se encontró un cáncer pilórico de 9 cm. de diámetro con extensión al duodeno y cabeza del pancreas. No se encontró metástasis a hígado, peritoneo, ligamento redondo del ombligo, cul - de - sac, omento, o ascites. La vena portal se separaba fácilmente de la masa tumoral al disecar el tunel intrapancreático. Se practicó una pancreaticodnodenectomía con la técnica descrita en el texto, con colecistectomía y omentectomía y hemigastrectomía. Se restableció continuidad intestinal con una pancreatico-yeyunostomía término-terminal, y dos anastomosis término-laterales con el jejuno, una con el colédoco y la última con el estómago. La pérdida de sangre en el procedimiento fue de 1,200 cc. El período postoperatorio transcurrió sin complicaciones mayores.

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Se proyecta tratar al paciente con quimioterapia adjuvante.

Discusión

El cáncer de estómago en Puerto Rico se ha mantenido con una incidencia alta, a pesar de que en los últimos diez años ha bajado la tasa a la mitad en Estados Unidos, al igual que en algunos países de Europa. Desde el 1971 al 1973 la tasa promedio de este cáncer en Puerto Rico era de 20.3 por 100,000 habitantes masculinos y de 8.8 por 100,000 habitantes femeninos. De esto solo el 1.7 por ciento en el hombre y el 3.0 por ciento en la mujer fueron reportados de origen pilórico (2, 3, 4). Es de interés notar que durante esos tres años no se reportó un solo caso de cáncer pilórico en el hombre en la región oeste de salud de donde provienen los dos pacientes presentados. También notamos que estos dos pacientes son de sexo femenino. Al analizar por la estadística de "Student" la hipótesis nula acerca de la significancia de la diferencia en esta tasa por sexo, encontramos que no hay diferencia significativa. Habría que analizar la hipótesis de nuevo cuando haya datos en años subsiguientes.

En cuanto a la técnica de la pancreato-duodenectomía queremos recalcar un punto que se describió recientemente (5), pero que habíamos descubierto independientemente hace algún tiempo antes en el Centro Médico de Mayagüez. Uno de los factores que limitan el proceder con esta operación es la invasión de la vena portal. En el pasado habíamos utilizado la portografía intraoperatoria para determinar este dato. Su interpretación era sumamente difícil en casos donde no había obstrucción franca de la vena, y sí había algún desplazamiento, haciéndose imposible diferenciar entre invasión de la pared y compresión sencilla por tejido adyacente. Para obviar esta dificultad, antes de dividir cualquier estructura que no le permita abandonar el procedimiento proyectado, Ejemplo, estómago, colédoco, o duodeno, y después de haber hecho una minuciosa exploración de vientre, se diseca, o con un instrumento o con el dedo, el canal portal a través del pancreas. La porción intrapancreática de la porta no recibe tributarias en su aspecto anterior o ventral, facilitando esta operación si uno se mantiene estrictamente en este plano. La disección comienza al despegar el omento del colon transverso, y así entrar en la transcavidad de los epiplones. Se sigue la vena cólica media hasta su confluencia con la vena mesentérica superior. Dividiendo la vena gastroepiploica derecha la mesentérica se sigue hasta su entrada al pancreas y aquí se sigue la disección en dirección cefálica por el aspecto, ventral de la vena. Comunicar el tunel así formado en la parte superior del pancreas cerca del extremo izquierdo del foramen de Winslow se facilita si uno diseca primeramente la arteria hepática, y divide dos de sus ramas, la arteria gastroduodenal y la arteria gástrica derecha Después de haber construído el tunel es fácil por palpación determinar infiltración de la vena y la extensión del tumor hacia esta estructura. La característica más deseable de este procedimiento es que le permite al cirujano desistir de la operación radical sin menoscabo a la integridad anatómica del paciente, a la vez que ofrece un máximo de información.

Si se decide proceder con la operación radical se puede efectuar una transección temprana del pancreas ya que la disección de su porción posterior se había completado. Esto es deseable porque le permite al cirujano ligar todos los vasos que confluyen con la porta o que ramifican de la arteria mesentérica superior, bajo visión directa y en su origen. Después de haber separado estos vasos grandes del especímen, se divide el duodeno del jejuno a nivel del ligamento de Treitz. Al traccionar el especímen hacia la derecha y hacia fuera el proceso uncinado del pancreas sale de su lecho y se puede cortar la facia de soporte a trasluz evadiendo y anticipando cualquier vaso sanguíneo. La disección de esta región antes de dividir el pancreas anteriormente y liberar los vasos grandes como se ha descrito, conlleva una disección tediosísima a través del proceso uncinado que le puede prolongar la operación por lo menos una hora al paciente y ocasionarle una pérdida de sangre considerable innecesaria.

Resumen

Se presentan dos pacientes con carcinoma del estómago originándose en el píloro con extensión al duodeno y la cabeza del pancreas. Se discute la incidencia, de este tumor en Puerto Rico, y sus características clínicas y patológicas. Se concluye que el mejor tratamiento es el de pancreatico duodenectomía si se determina intentar una resección curativa.

Se describe la técnica de la disección de la porta intrapancreática y su uso en la evaluación intraoperatoria del paciente con cáncer en esta región. También se enfatiza el uso de este abordaje en la disección

del proceso uncinado del pancreas.

Summary

Two patients are presented with carcinoma of the stomach originating in the pylorus with extension to the duodenum and head of the pancreas. The incidence of this tumor in Puerto Rico is discussed, along with its clinical and pathologic characteristics. We conclude that the best treatment is a pancreatico-duodenectomy, if it is determined that a curative resection can be done.

The technique of dissection of the intrapancreatic portal canal is described along with its use in the intraoperative evaluation of these patients. We also emphasize the use of this approach in the dissection of the uncinate process of the pancreas.

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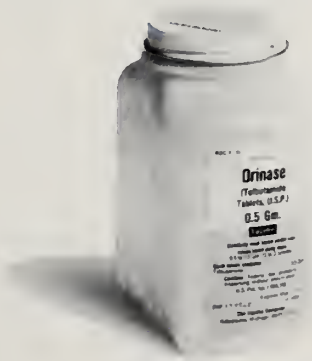
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TRATAMIENTO CON CYPROHEPTADINE EN UN CASO RECURRENTE DE ENFERMEDAD DE CUSHING

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El origen de la enfermedad de Cushing a nivel del sistema nervioso central se deduce de la experimentación y se ha podido probar que la serotonina tiene un papel importante en la regulación de la liberación de corticotrofina (ACTH) (1, 3).

En general el tipo de tratamiento específico empleado actualmente en la enfermedad de Cushing es quirúrgico o consiste en algún tipo de irradiación. Las complicaciones de la terapéutica quirúrgica pueden ser: rinorrea de líquido cerebroespinal, daño al nervio óptico, hormonas tróficas y antidiurética. La morbilidad y mortalidad son mayores que con la radioterapia, de ahí que la cirugía se reserve para los casos en que no pueda emplearse la radioterapia. Existen tres métodos para dirigir la radioterapia a la glándula pituitaria (2):

1. El método clásico que consiste en el uso de irradiación convencional externa en dosis de 3,000 a 5,000 Rads administrada en varias semanas.
2. La irradiación interna de la pituitaria por medio de la implantación esterotáctica de proyectiles en forma de Ytrium, y usando la vía transnasoesfenoidal.
3. La técnica más reciente consiste en el uso de partículas alfa (protonbean) de una fuente de irradiación externa. Por este método pueden administrarse hasta 12,000 Rads en la glándula pituitaria sin que se haya podido demostrar evidencia de daño a las estructuras circundantes. Esto se consigue al poder enfocar el rayo más precisamente que con la técnica de irradiación gamma y al poder usar múltiples accesos. Aún con esta técnica tan refinada hay una gran incidencia de parálisis oculomotora.

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Los pacientes con formas severas de Cushing no son candidatos a la irradiación externa. El retraso que hay entre el tratamiento y la remisión y el hecho de que las posibilidades de remisión son menores de 50 por ciento contraindican este tipo de terapéutica en casos de enfermedad rápidamente progresiva.

Un informe reciente ha demostrado que el tratamiento de la enfermedad de Cushing con cyproheptadine (Periactin ®) que es una droga antiserotonina, se asocia con una pronta mejoría en la clínica y en los parámetros de laboratorio. En vista de la eficacia y la aparente ausencia de toxicidad, este agente parece ofrecer un tratamiento prometedor, y está basado en la neurofarmacología química de la regulación de la liberación de ACTH.

Considerando la recurrencia en un caso de la enfermedad de Cushing, después de haber empleado varios métodos terapéuticos decidimos hacer una prueba con cyproheptadine con el propósito de alcanzar un control tanto clínico como químico para beneficio del paciente.

Sujeto y Método

Este es el caso de una paciente de 29 años de edad que en el 1963 presentó un cuadro clínico de Cushing con obesidad truncal de aparición súbita, amenorrea, hirsutismo, estrías, acné y debilidad. Presentaba además dolores de cabeza de tipo occipital, poliuria, polidipsia sin antecedentes de ingestión de esteroides (Fig. 1).

En la evaluación preliminar se encontró tensión arterial alta (180/120), diabetes mellitus y el diagnóstico de hiperplasia adrenal fue bien documentado. En noviembre de 1963 se le hizo adrenalectomía subtotal, presentando un episodio de insuficiencia adrenal transitoria. Se reevaluó el caso en 1964 y se encontró evidencia clínica y química de hiperplasia adrenal, no autónoma del tejido remanente. En el 1965 se hizo adrenalectomía total y se puso en dosis de mantenimiento de cortisona, pero se perdió en su seguimiento hasta 1967 en que vino con un cuadro florido de Cushing. En esta ocasión se encontró tejido adrenal hiperplástico que suprimía su actividad a 8 mg de dexametasona. Se hizo una prueba clínica con Elipten pero falló la supresión y presentó efectos secundarios de tipo gastrointestinal severos.

TABLA I
PARAMETROS SEGUIDOS EN EL TRATAMIENTO CON CYPROHEPTADINE

Fecha	Dosis de Cyproheptadine (mg/d)	Peso (libra)	Tensión Arterial (mm hg)	Glucosa en suero (pp mg °/o)	K + Sérico (meq/L)	Cortisol libre orina 24 hrs. (mcg/ 24 hrs.)
2/9/76	0	141.5	138/108	324	3.7	554
2/11-3/11/76	8 mg bid	139	130/98	185	4.7	610
3/11-3/23/76	16 mg bid	139	120/84	225	4.5	200
3/23-5/7/76	12 mg bid	138 1/2	120/80	205	4.4	56



Figura 1: *La paciente en 1964.*

Desde 1968 hasta 1973 continuó presentando manifestaciones de enfermedad de Cushing activa con hiperglicemia, hipertensión moderada, hirsutismo e hiperpigmentación. Se le dio un curso de radioterapia desde mayo 7 hasta junio 12 de 1973 con una dosis total de 5,000 Rads de ^{60}CO.

Se recvaluó el caso en el 1974 y se encontró que aqucjaba dolores severos dc cabeza, menstruación regular, hiperpigmentación, hirsutismo y debilidad muscular generalizada, además de hipertensión moderada (150/100) e intolerancia a los carbohidratos.

Debido a lo refrăctario del caso se consideró la radiación con partículas alfa (protombean) pero, por la gran cantidad de irradiación a la pituitaria el administrar radiación adicional conlleva riesgos quc incluyen entre otros visión doble y el posible desarrollo de defectos mínimos en los campos visuales, Se recomendó esperar por lo menos 3 años antes de intentar la irradiación con partículas alpha. En lo que se esperaba se decidió hacer una prueba terapéutica con cyproheptadine considerando los buenos resultados obtenidos por el grupo de Krieger (1).

Métodos y Resultados

Se hicieron pruebas basales y evaluación clínica antes de comenzar el estudio. El caso se siguió con cortisol libre en orina de 24 horas y azúcar en sangre 2 horas post prandial mensualmente durante el estudio.

Se recomienda una dieta de 1,200 calorías diabética y se siguen los parámetros de peso, glucemia post prandial, potasio, cortisol urinario y tensión arterial.

El cyproheptadine se administró por boca en dosis dividida, gradualmente aumentando de 8 a 24 mg. por día. El estudio se planeó para tres meses al cabo de los cuales el paciente continúa en dosis de mantenimiento de 24 mg de cyproheptadine diario (1).

La Tabla I nos demuestra los resultados obtenidos antes y después del tratamiento con cyproheptadine.

Discusión

Nuestra experiencia obtenida con la administración de cyproheptadine se asoció con una pronta normalización de los niveles de cortisol libre en orina. No demostró cambios significativos con relación a sus dolores de cabeza, pigmentación, hirsutismo u obesidad. La tensión arterial se normalizó sin el uso de medicación específica.

La persistencia de hiperglucemia nos sugiere una diabetes genética y no secundaria al exceso de glucocorticoides.

La enfermedad de Cushing en la actualidad se considera como el resultado de alteraciones en la función del sistema nervioso central, lo más probable una alteración en la concentración de neurotransmisores o una sensitividad anormal con respecto a la liberación de ACTH. Cyproheptadine es una droga con efecto antiserotonina, antihistamínico y anticolinérgico, pero, en la dosis empleada en este estudio, los efectos antiserotonina son los beneficiosos (1, 3).

El efecto de la radioterapia previa con ^{60}CO no puede cuantificarse, de ahí que se sugiere la posibilidad de una alteración neuroquímica por lo cual no pueda observarse una mejor respuesta clínica al medicamento. Se requiere más experiencia con este tipo de tratamiento y estudios más controlados que puedan definir si es de mayor beneficio clínico cuando se administra antes de la irradiación. Esta modalidad de tratamiento que resulta económico, fácil de llevar y que apenas presenta efectos secundarios debe aceptarse y emplearse con más frecuencia.

Resumen

Tuvimos la oportunidad de estudiar un caso recurrente de la Enfermedad de Cushing, en el cual probamos el efecto antiserotonina de cyproheptadine. Pudimos normalizar los niveles urinarios de cortisol y conseguimos una mejoría en la tensión arterial, pero no en los demás parámetros. Recomendamos más investigación y experiencia clínica con esta nueva y fácil modalidad de tratamiento.

Summary

We had the opportunity to study a case of recurrent Cushing's disease. We proved the antiserotonin effect of cyproheptadine. We achieved the normalization of urinary free cortisol and improvement on the blood pressure. We recommend more clinical experience and investigation with this new and easy modality of treatment.

Reconocimiento

Esta paciente fue evaluada y tratada de 1963 a 1974 en la Sección de Endocrinología del Hospital Universitario, bajo la hábil dirección de la Dra. Lillian Haddock.

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CENTRO MEDICO DE MAYAGUEZ
QUINTO ANIVERSARIO

"El primer hospital nació de apuro, de la caritativa mano de Faviola, hace como quince siglos, y para solucionar un problema".... (1). Como el primer hospital han surgido todos, con un objetivo, con una finalidad: dar servicio que constituye un derecho ciudadano.

Surge la necesidad y hombres y mujeres anónimos, preclaros, de la región claman por un derecho que comienza a ver luz para los años 1957 y 1958 cuando se aprueba la asignación de fondos por las Resoluciones Conjuntas de la Cámara Núm. 92 y Núm. 917, asignando dinero para la compra de terrenos donde se ubicará el Hospital de Distrito de Mayagüez. El Representante Hon. Benjamín Cole crea los proyectos y consigue de la Administración Municipal la asignación de los $150,000 restantes para la compra de los terrenos y los gastos estudios que montaban a $300,000. Con estas raíces prende el fruto, y el 1ro. de junio de 1960 es firmada la Ley Núm. 17, presentada en la Cámara por el mismo Representante Cole, por el entonces Gobernador de Puerto Rico Honorable Don Luis Muñoz Marín, creándose el concepto y autorizando la construcción del Centro Médico de Mayagüez.

La facultad médica y paramédica del Hospital de Distrito de Aguadilla vendrá a llenar la institución que una vez construída permanece cerrada por espacio de dos años. A comienzos de 1971 da sus primeros signos de vida con algunos servicios aislados; en febrero de ese año, el día de la Virgen de la Candelaria, se inaugura oficialmente el Hospital pero este no comienza a prestar servicios de hospitalización hasta junio del mismo año cuando se muda a toda prisa el Departamento de Pediatría, y posteriormente los miembros de los otros departamentos. La Facultad Médica de Aguadilla constituye el verdadero precursor y germen de nuestra Facultad, persistiendo muchos de ellos en la actual. Traen consigo dos programas de Residencias aprobadas, Pediatría y Ginecología y Obstetricia. Posteriormente se sumaron, ya en Mayagüez, Medicina y Cirugía.

Prestará el Hospital Dr. Ramón Emeterio Betances, servicios curativos de excelencia a la región, a la vez que colaborará en diversos programas de Medicina Preventiva. Trae a Mayagüez un sinnúmero de especialistas en áreas que antes no disponía la región, e incluso inexistentes y muy escasos en otras áreas de Puerto Rico, y más que nada, provee más facilidades públicas para el paciente indigente que en aquel momento solo disponía del Hospital San Antonio (Municipal), el Hospital de Distrito de Aguadilla, algunos hospitales municipales pequeños de las localidades vecinas, y de la buena voluntad de algunos caritativos médicos privados de la región.

Establece el paso de la educación médica de la región, entrenando médicos en su internado, y creando especialistas en las áreas de Pediatría, Cirugía, Ginecología y Obstetricia y Medicina Interna. Especialistas que han ayudado, y están ayudando, en estos años a disminuir la carencia de personal especializado en toda la región. Facilita la adaptación a nuestro sistema médico a graduados de escuelas extranjeras mediante programas noveles de "Quinta Trayectoria", "Curso teórico-práctico". "Octavo semestre" y finalmente se une en consorcio con la Escuela de Medicina de Puerto Rico permitiendo que nuestros estudiantes reciban su enseñanza clínica en el área que luego han de prestar sus servicios. Estudiantes nuestros y extranjeros, de las Universidades de Navarra (España), Guadalajara (México) y Pedro Henríquez Ureña (República Dominicana) reciben su educación de último año en nuestras facilidades.

Tras cinco años de labor, nos visitan conferenciantes invitados del país y del extranjero, y los nuestros se desplazan de la misma forma. Las publicaciones científicas nacionales e internacionales comienzan a aparecer en número significativo.

La institución ha atravesado por problemas de índole económica-administrativa, pero tiene vida científica, moral y laboriosa. Su personal no pide salarios, sino mejorar las condiciones de trabajo. Constituye la primera institución de servicios médicos en la Isla, donde tanto médicos como enfermeras luchan por aumentar las facilidades de servicio sin pedir más salarios. Nuestros empleados enaltecen la institución y la sirven, no la explotan.

Los cinco años han sido duros, pero han merecido la pena. La facultad médica y paramédica unida sigue un derrotero firme hacia un futuro lleno de esperanza para la institución, sus miembros, y más aún, los pacientes. Por ello ha luchado y lo seguirá haciendo.

Nos honra servir como Presidente de esta facultad, a los principios para los que fue creada, y por ella lucharemos mientras nos sea permitido y nos sea posible.

Queremos recordar unas palabras útiles y sinceras, que nos serán de utilidad en la planificación del futuro: "Los progresos que ha alcanzado la salud de los grupos humanos en el período contemporáneo se deben en escasa medida a la medicina curativa, a pesar de los espectaculares avances que la terapéutica ha conseguido. Mucho mayor es la participación que corresponde a la Medicina Preventiva, pero conviene tener en cuenta que la parte más importante del progreso sanitario se debe a factores no directamente médicos. El fomento de la salud depende, en efecto, de los avances económicos, políticos y sociales de tipo general." (2).

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FACTORS THAT MAY BE OF HELP TO POINT OUT WHICH PATIENT HAS A HIGHER RISK OF DEVELOPING CARDIOGENIC SHOCK (RISK FACTORS FOR CARDIOGENIC SHOCK)

Henry Mayo Rojas, MD, Luis A. Román, MD, FACP, San Juan City Hospital, Department of Medicine, Cardiology Section.

This is a preliminary report of a retrospective study in 120 consecutive patients with acute myocardial infarction admitted to our Coronary Care Unit for a period of 15 months, (December 1, 1974 to February 29, 1976). 27 different parameters were studied to point out which of them could be of help to select the higher risk patient for developing cardiogenic shock. This includes: sex, age, the major risk factors for coronary disease, location of M. I., arrhythmias, the routine laboratory work-up in patients with M. I., the need of temporary pacing, C. V. P. values, complete history and physical exam data, amount of antiarrhythmic medication given, etc. Comparison was done with 15 patients who died in cardiogenic shock during 1973. Of the 120 patients, 90 were males (75 percent) and 30 females (25 percent). Mortality was 15 percent (18 patients).

Of the 27 different parameters studied, the following were of greatest value in determining which patient had a higher risk of developing cardiogenic shock. 1) age above 70 and/or, 2) the presence of hypertension, diabetes mellitus and obesity, 3) if the infarction was anterolateral in location, 4) no previous angina or if in unstable angina upon admission, 5) signs and symptoms of congestive heart failure, 6) the presence of bifascicular block, 7) cardiomegaly on admission, 8) persistent sinus tachycardia and P.V.C.'s.

ACUTE MYOCARDIAL INFARCTION: MANAGEMENT AND OUTCOME IN FOUR HOSPITALS

Francisco Jaume, (Member) Arminda E. Rodríguez, M.D., Gilberto Veray, M.D., Francisco Ojeda, M.D., Mayagüez, Puerto Rico.

The medical records of patients admitted from January 1971 to December 1975 with documented myocardial infarction at three Mayagüez private hospitals and at the Mayagüez Medical Center were studied. Correlation between clinical picture, complications, and mortality were made. Patients treated in the intensive care unit are compared with those treated outside these facilities. The length of the hospital stay of those who survived is analyzed. Specific recommendations are made based on our experience for improving the medical management that may modify favorably life expectancy.

NORMAL AND ABNORMAL RESPONSE TO MAXIMAL GRADED EXERCISE

Don R. Rivera, M.D., (Member), Fernando Defilló, M.D., (Member), Félix M. Cortés, M.D., F.A.C.P., Ponce District Hospital.

Maximal Exercise Stress Test was carried out in 56 patients using Bruce Protocol. Normal controls-10 cases (6 athletes). 46 patients studied for chest pain. 37 had no evidence of Ischemic disease for the level of exercise performed, 9 developed Ischemic ST Segment changes. The following observations were made: 1. Normal curves for BP, HR, product of HR-Systolic -BP (HR-S) response to graded exercise (Bruce Protocol) have been constructed. 2. The level of Stress on the Cardiovascular System as judged by (HR-S) or level of exercise performed was greater in the trained athlete than in the normal untrained subjects, followed by patients with the Ischemic response. 3. Ischemic ST.

Segment response occurred one stage before the onset of chest pain in 3 subjects. 4. In 2 patients studied after coronary by pass surgery-Ischemic ST. Segment response appeared at the same stage as the preoperative study, but failed to develop chest pain during the post-operative study. 5. P-Terminal force became prominent in the Post Exercise Tracing in 4 patients with Ischemic Heart Disease-suggestive of Acute Left Atrial overload. 6. Arterial Blood Gases immediately after the study showed Mild Metabolic Acidemia with Normal O_2 tension. 7. Female patients achieved a lesser degree of Stress but the physiologic response to maximal stress exercise are identical to the male at the level exercised achieved. *. Maximal or sub-maximal Stress Test is informative not only in Ischemic Heart Disease, but to evaluate the functional state of the subject as to the Musculo-Skeletal, Pulmonary, Cardiovascular System, as well as to some Psychophysiological CV disorder.

THE CLINICAL USE OF ECHOCARDIOGRAPHY IN THE TIMING OF HEART SOUNDS

Francisco Olazábal, Jr., M.D., Aureo Calderón, M.D. and Roberto Rodríguez, M. D., Industrial Hospital, Department of Medicine, Puerto Rico Medical Center.

In the past one had to rely on the use of the electrocardiogram, the apexcardiogram or pulse tracing recordings for the identification of phonocardiographic events in the cardiac cycle. This has caused difficulties because of the time delays involved, either in the relationship of electrical and mechanical events, or in the slow propagation of pulse waves through tissue or blood. The application of ultrasound echocardiography permits the simultaneous correlation of mechanical and auditory events, since for clinical purposes, both sound and ultrasound have similar conduction velocities. In the past year over 50 patients have been evaluated with the simultaneous recording of heart sounds, electrocardiogram, echocardiogram and either apexcardiogram or pulse tracings. These patients had presented problems in the identification of auditory events. The importance of the addition of the echocardiogram in the timing of heart sounds is demonstrated and examples of its value given with illustrative case reports. The future clinical importance of these findings is stressed.

SINDROME DE CUSHING: EXPERIENCIA CLINICAL A TRAVES DE 25 AÑOS

Efraín Meléndez, M.D. (Associate) and Agustín M. De Andino, F.A.C.P., Departamento de Medicina Interna, Hospital Municipal, San Juan, P. R.

Durante los últimos 25 años hemos observado un total de 7 casos del síndrome de Cushing en el Departamento de Medicina Interna del Hospital de la Capital y en la práctica privada de uno de los autores (AMA). La serie consiste de 6 mujeres y un varón con una variación en la edad de 16 a 44 años y una edad media de 31. La duración de la sintomatología se extendió desde 3 meses hasta 10 años. La sintomatología más prominente fue la neuropsiquiátrica variando desde la inestabilidad emocional leve hasta episodios de epilepsia grand mal y sicosis orgánica severa de tipo maníaco depresiva y/o esquizofrénica. Otros síntomas de importancia en la mujer fueron la amenorrea y el hirsutismo. Todos mostraron obesidad variable. Hipertensión arterial se observó en todos los casos menos uno. Disturbios en el metabolismo de carbohidratos que fluctuaba entre diabetes severa insulinoresistente y anormalidades en la tolerancia de glucosa se hallaron en toda la serie. Ninguno de los pacientes mostró osteoporosis. Todos los casos (con la excepción de dos en los cuales no se hizo la determinación por no existir facilidades del laboratorio) demostraron elevaciones en los niveles urinarios de 17-hidroxicorticoides. Elevaciones en el cortisol plasmático y ausencia en el ritmo circadiano del mismo se encontró en los dos casos recientemente estudiados.

Los diagnósticos patológicos en los casos intervenidos fueron de hiperplasia adrenal en 4, carcinoma adrenal en 1 y adrenal normal en 1 caso sometido solamente a operación exploratoria adrenal con biopsia unilateral. El caso número 7 mostró un adenoma pituitárico y está aún bajo evaluación luego de haber recibido un curso de radioterapia.

HYPERLIPOPROTEINEMIC TYPES AMONG PUERTO RICANS: A FINAL REPORT

Marta Cancio, Ph.D. and José M. León, B.S., M.T., General Medical Research Laboratories, VA Hospital, San Juan, Puerto Rico.

This report summarizes the results of a study on hyperlipoproteinemic Puerto Rican subjects performed during an eight year period. Classification in types was done according to the World Health Organization. Distribution of cases by type was: 5 Type I, 258 Type IIa, 198 Type IIb, 186 Type IV, and 76 Type V. Type I were all children of Caucasian race; 4 females, 1 male. Type IIa were mostly in their fifties, while Types IIb, IV and V peaked in number in their forties. Over 90 percent of cases in all types except Type V were Caucasian; in Types IIa, IIb, IV and V close to 90 percent or over of cases were made. In type IV 78 percent were obese and 67 percent were diabetic. These conditions were also high (over 60 percent) in Type V. CVD was high (over 60 percent) in Types IIa and IIb. Over 60 percent of the cases of all types were from the Northern region of Puerto Rico.

TROPICAL FISH POISONING:- CIGUATERA IN PUERTO RICO

Charles A. Payne, M.D., F.A.C.P. and Sylvia N. Payne, M.D.

Historical evidence of tropical fish poisoning dates to Egyptian carvings as remote as 2,700 B.C. The problem exists today apparently in a similar form and is quite prominent in the waters of the West Indies, including Puerto Rico. Ciguatera, or ciguatoxin, is the most important type locally because of its potential severity. A similar if not identical variety exists in the Pacific and has been studied extensively. The disease is a variety of fish flesh poisoning (icthyosarcotoxism) which effects unsuspecting humans with a variety of gastrointestinal and neurological signs and symptoms which frequently go undiagnosed since little is known about the entity. Many major textbooks fail to mention it at all.

Varieties of tropical fish poisoning will be discussed and the role that marine neurotoxins have played in neuromuscular research, especially nerve membrane and junction physiology, will be described. A series of recent cases collected by the authors will be presented.

A REVIEW OF THE ASTHMA MORTALITY FROM 1972 TO 1973 IN PATIENT ADMITTED TO SAN JUAN CITY HOSPITAL, DEPARTMENT OF MEDICINE

José N. Moreno, M. D.

In 1972 a total of 52 patients with the diagnosis of bronchial and/or status asthmatious were admitted to the San Juan City Hospital, Department of Medicine. Of these, 11 were admitted with the diagnosis of status asthmatious and 41 with bronchial asthma. Out of these 52 patients, 4 patients died (7.7 percent).

In three of the four patients who died, the use of sedatives was the most important factor responsible for the death of the patients. The four patients died of an extensive bronchoneumonia and respiratory failure.

In 1973 a total of 37 patients were admitted, seven with status asthmaticus and 30 with bronchial asthma. Out of these 30 patients, three patients died (8 percent). In two patients excessive use of sedative medication was responsible for death of the patient and it might have contributed to the death of the third patient, who had extensive confluent bronchopneumonia and bronchiectasis.

It has been stated that in Puerto Rico the incidence of bronchial asthma and the mortality from asthma is twice as much than in the U.S.A. Our study revealed that there are several factors which contribute to the mortality, in particular the use of sedatives.

SURVIVORSHIP IN SYSTEMIC LUPUS ERYTHEMATOSUS: ANALYSIS OF 284 CASES.

Esther N. González-Parés (FACP) and Rodolfo Concepción (by invitation). Puerto Rico School of Medicine, San Juan, Puerto Rico.

Clinical studies of Systemic Lupus Erythematosus (SLE) have established that survivorship declines from the time diagnosis is first made. Survival time following diagnosis of SLE was studied in 284 patients between the ages of 4 to 63 years.

There were 252 females and 32 males. Survivorship, in the total patient series, declined most in the first year. At the end of the first year, the cumulative survival rate (CSR) was 85 percent and continued

to delcine to a CSR of 73 percent and 70 percent after 5 and 10 years respectively. The 10 yr. CSR for the group before 15 was 74 percent.

Eighty four patients (29.6 percent) died; of these 13 were children. Of all deaths, 55 percent occurred within the first year, and only 9.5 percent occurred after 5 years of diagnosis. Renal involvement was scen in 187 patients (65.8 percent), of whom 72 patients died. Central nervous system involvement (CNS) was seen in 67 patients of whom 27 patients (42.9 percent) died. Heart involvement was present in 99 patients of whom 51 died (51.8 percent).

The foregoing data indicates that the most critical years for survival are the first 5 years after diagnosis. In males the disease occurred much less frequently, was less severe and carried a lower mortality than in females. When the diagnosis was established before diagnosis was established after age 15. Survivorship was affected by the frequency of renal, heart and CNS disease. Patients with heart or CNS involvement had the lowest CSR at 5 years.

DNA ANTIGEN BINDING AVIDITY AND NEPHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Julio E. Lergier, F.A.C.P., Esther N. González-Parés, F.A.C.P., Raquel Martínez, (Associated Member), and Carlos Fernández, (Associated Member), University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

Previous studies from this laboratory have shown a correlation between very high titers of anti-native deoxyribonucleic acid (nDNA) antibodies (AB) and active, severe nephritis in patients with systemic lupus erythematosus (Bol Asoc Méd PR 67: 323-324, 1975). Some patients with high n-DNA binding did not manifste severe penhritis during their course and therefore studies of nDNA antigen binding curves by SLE sera were analyzed to compare nDNA binding avidity differences which could explain this observation. Six (6) SLE patients with high n-DNA binding ($>$ 10 micrograms/ml) and severe nephritis were compared to six (6) SLE patients with high n-DNA binding but minimal (2) or no nephritis (4). Three (3) normal sera ($<$ 2.5 micrograms/ml) were used as controls. N-DNA antigen binding avidity as measured by *slope* determination was significantly higher in patients with severe nephritis (mean = 755.2 mcgm/ml) than in those with mild or no nephritis (mean = 101.9 mcgm/ml) or in normal sera (mean = 6.6 mcgm/ml). These finding suggest an enhanced DNA-antiDNA immune complex formation due to increased antigen binding avidity as a possible explanation for observed differences in the incidence and severity of nephritis in SLE patients.

HYPERURECEMIA AND ACUTE RENAL FAILURE

José Martinó-Trilla, Manuel Martínez Maldonado, F.A.C.P., Veterans Administration Center, San Juan, Puerto Rico

Hyperuricemia above 12 mg percent is not an usual finding in acute renal failure. The only exception to this which is readily identified is in subjects suffering from lymphoproliferative or myeloproliferative disorders, given chemotherapy. We have recently seen 4 patients in whom acute renal failure co-existed with hyperuricemia with levels above 15 mg percent.

All the subjects were alcoholics and upon admission to the hospital were found to have hyperbilirubinemia. Another interesting feature was the fact that at least two of the subjects had had episode suggestive of acute pancreatitis. Three of the four subjects recovered from acute renal failure and had spontaneous return of uric acid levels to normal. The course of the disease and other characteristics of their clinical picture did not differ significantly from that seen in other cases of acute renal failure of known etiology. The most significant difference was an elevation in the ratio of the clearance of uric acid to the clearance of creatinine in the two subjects in which it was measured. In these two patients, the ratio exceeded unity. Most subjects with acute renal failure have ratios less than 1. The possibility that the hyperuricemia was the consequence of some aspect of alcoholism will be discussed. The use of uric acid fractional clearance can help distinguish hyperuricemic acute renal failure from acute renal failure of other causes.

CHRONIC PERSISTENT HEPATITIS IN PUERTO RICO

Esther A. Torres, M.D. (Associate), Pedro H. García Pont,

M.D., San Juan Veterans Administration Hospital, San Juan, Puerto Rico.

The records of patients with the histologic diagnosis of chronic persistent hepatitis were examined to review the clinical experience in our hospital with this entity. A list of 27 patients was obtained from a review of all liver biopsies performed between 1968 and September 1975, of which 14 records were revised. Age at onset ranged from 22 to 65. Seven patients had jaundice as the main manifestation. Hepatomegaly was present in 7. No patient showed evidence of chronic liver disease or hepatic decompensation. Ten had previous episodes of jaundice. Drug addiction was present in 5; 3 had received blood transfusions. HB Ag was positive in 2 of 11 patients tested. Abnormalities in the liver function tests wree present in all. Liver-spleen scan was abnormal in 2 of 10. Of 8 patients followed up for more than one year, none has progressed to chronic liver disease.

Experience with this entity is not abundant in the literature. However, our small series seems to follow the expected previously described pattern. Extended follow up of all patients with this diagnosis and further investigation of this entity are warranted.

THE TARSAL TUNNEL SYNDROME

Alejandro E. Franco, M.D. (Member), Rafael Berríos Martínez, M.D., Radamés Sierra, M.D., Ricardo Méndez Bryan, M.D. Instituto de Reumatología de P. R. and Department of Physical Medicine, School of Medicine, San Juan, P. R.

The tarsal tunnel syndrome (T.T.S.) was established on 1962 by Keck (J. Bone Joint Surg 44 A 180, 1962) to designate the wide variety of symptoms and signs caused by the compression of all or part of the posterior tibial nerve as it passses through the inelastic fibro-osseous tunnel inferior to the medial malleolus. The T.T.S. is not frequently recognized and the largest published series is of 10 patients.

At the Instituto de Reumatología de P. R. we have diagnosed a T.T.S in 5 patients, in 1 bilaterally. In all patients the diagnosis was confirmed by nerve conduction velocity studies.

The age range of our patients is 41 to 53 years, 3 are females, 2 males. Symptoms were localized to the sole of the foot; 4 patients complained of pain radiating to the calf and 1 of numbness.

In 3 cases the Tinels sign was positive. Laboratory and radiologic studies were not contributory. No evidence was detected of systemic disease, except for osteoarthritis in 1 patient and overweight in 2.

Comparison of our patients with those published in the literature will be presented.

THE EEG IN DIALYSIS DEMENTIA

A. Noriega Sánchez, M.D., G. Saleh, M.D., O. Ramírez Muxó, M.D. (Member), R. Ramírez González, M.D., C. Pérez, EEG Tech., Department of Medicine, VA Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

A fatal encephalopathy associated with hemodialysis has been recently described.

All twelve patients in the literature have died. Trace metal analysis has demonstrated high aluminum levels in the brains of some cases, but the etiology remains undetermined. The only test which clearly differentiate patients with this encephalopathy from others is the EEG.

With the purpose of identifying which patients in our unit were susceptible to develop this complication, we performed EEG's on all who were on dialysis for more than 2 years. Nine, out of 45, were found to have paroxysmal bursts of slow waves, sharp waves, triphasic waves, and sometimes, spikes similar to the cases in the literature.

All nine patients underwent standard neurologic testing. Six patients had signs and symptoms indistinct from those reported with Dialysis Dementia. The findings included dementia, speech disturbances, involuntary movements and seizures. Three were free of symptoms and subsequently became symptomatic. One patient four months after the initial positive EEG; one two months, and the other 6 weeks afterwards. Two of these three cases died and the other is progressively deteriorating.

Our study suggests that routine EEG's in Hemodialysis Units helps in anticipating this syndrome.

THE CLINICAL AND LABORATORY ASSESSMENT OF HYPOGLYCEMIA: REPORT

OF THE FIRST PATIENT WITH AN INSULINOMA AT THE UNIVERSITY DISTRICT HOSPITAL

Francisco Aguiló, Jr., M.D., F.A.C.P.

During the last 12 years we have made a systematic evaluation of all adult patients presenting with hypoglycemia (true blood sugar below 50 mg/dl.), in order to establish its etiology and institute specific therapy whenever possible.

Clinical History, physical examination, routine laboratory tests, plus prolonged fasting, oral glucose tolerance, leucine and I. V. tolbutamide tests have been done in at least 30 patients, utilizing measurement of immunoreactive insulin. Studies on 12 of these will be presented. Most patients were found to have "reactive hypoglycemia", approximately half of which had preceding hyperglycemia and (or) hyperinsulinism during oral glucose tolerance tests. One patient was found to have early Addison's disease.

Finally, a 60-year old female with an 8 year history of "psychiatric" disorders was found with documented fasting hypoglycemia and hyperinsulinism, increased I/G ratio, exaggerated insulin response to oral glucose, intravenous glucose, oral leucine and intravenous tolbutamide tests. A 3.5 x 2.5 cm mass, visualized by coeliac arteriography, was removed surgically and was confirmed by light and electron microscopy to be a beta-cell adenoma.

Post operatively, the patient developed a pseudocyst and became permanently diabetic, requiring insulin administration.

A review of highlights of the world literature on insulinomas will be presented.

PLASMA RENIN ACTIVITY AND BLOOD PRESSURE REGULATION IN DIABETES MELLITUS

Laura Lespier-Dexter, M.D., Carlos Guerra-Santiago, M. D., and Manuel Martínez-Maldonado, M.D., F.A.C.P., VA Hospital, San Juan, Puerto Rico.

An intact renin angiotensin system is required for hemodynamic adjustment to upright tilting in sodium depleted normal subjects. Impairment in this system has been reported in diabetic patients with or without nephropathy, autonomic neuropathy or orthostatic hypotension. Blood pressure (BP) during mechanical tilting, plasma and blood volume (BV) as measured with ^{131}I Human Serum Albumin, plasma renin activity (PRA) and the interrelation among these parameters was studied in a group of diabetic patients while on regular, 10 mEq Na^+ –60 mEq K^+ , and 150 mEq Na^+ –60 mEq K^+ diets. During sodium deprivation, there was a significant drop in plasma volume from 2451 ml to 2082 ml. Postural and volume response of PRA was blunted but within normal range. BP decreased significantly during tilting maneuvers. Mean baseline recumbent was 172/92 mmHg; mean minimal during tilting 103/67 mmHg. Impaired responsiveness of PRA does not seem to be the factor responsible for orthostatic hypotension of diabetes mellitus in the patients studied. Compromised baroreceptors and chemoreceptor reflexes in the presence of decreased intravascular volume are probably of more etiologic importance. Hypoalbuminemia, impaired renal volume regulatory mechanism or injudicious use of diuretics, conditions associated with a diminished intravascular volume, increase the risk of significant orthostatic hypotension in some diabetic patients.

HUMAN FASCIOLASIS: FIRST REPORT IN THE ISLAND LITERATURE.

E. López-Enrique, M.D., H. Galib-Frangie, M.D., C. Ramírez-Ronda, F.A.C.P., University of Puerto Rico School of Medicine, San Juan Puerto Rico.

The first reported case of infestation with *Fasciola hepatica* acquired in Puerto Rico is presented. The presence of cattle and of the molusk of the genera Lymnae in our soil, the moist tropical climate and the recent proliferation of household vegetable gardens in Puerto Rico combined themselves to make our environment an ideal one for the promulgation of this clinical entity. The clinical presentation of the condition is non-specific with fever, general malaise, decrease in appetite and hepatomegaly. Some cases may present with jaundice. The diagnosis of the condition is made by the presence of *Fasciola hepatica* eggs in the stools.

The diagnosis can also be corroborated with measurement of antibody titers against *Fasciola hepatica* by counterimmunoelectrophoresis. Epidemiologic data that help in the diagnosis is a history of ingestion of fresh vegetables grown in marshy waters. The treatment is with bithional or emetine hydrochloride and should be carried by a specialized center. The best of treatments is prevention. We want to alert the Puerto Rican medical community about the problem of human fasciolasis. We will present the approach to prevention, recognition, diagnosis and management of the clinical entity.

LONG TERM REMISSION OF HYPOCALCEMIA POST VITAMIN D THERAPY IN A PATIENT WITH PSEUDOHYPOPARATHYROIDISM.

Vilma Rabell, M.D. and Lillian Haddock, M.D., FACP (Member), Dept. of Medicine, UPR- School of Medicine.

A 52-year old female was admitted in hypocalcemic tetany to the University Hospital in October 1973. Physical examination was unremarkable. The serum calcium was 6.6 mg/dl the serum phosphorus 6.3 mg/dl and the serum magnesium 1.6 mg/dl. Renal function was normal and she had no evidence of malabsorption. Parenteral PTH administration failed to increase the serum calcium and the urinary phosphorus. The plasma PTH done by radioinmunoassay was 46 ulEq/ml (normal 15ulEq/nl). A diagnosis of pseudohypoparathyroidism was made and she was treated with vitamin D_2 from November 1973 to December 11, 1974 when she became hypercalcemic. One year after the D_2 was discontinued the patient was still eucalcemic. Serial 25 OHD levels were performed in this year period and when last performed on May 1976 was two and a half times the control value.

The response to PTH was repeated while eucalcemic. This time she responded with an increase in the serum calcium to a hypercalcemic level and adequate phosphaturia. The 25 OHD level was doubled upon PTH administration.

Documentation of normalization of the response to PTH after vitamin D therapy has been documented in Pseudohypoparathyroidism but not so a long term remission. In this respect this patient represents a most unusual occurrence.

The implication and significance of this finding will be discussed.

Q FEVER IN PR: A CASE REPORT

C. León-Valiente, (Associate), C. H. Ramírez-Ronda, F.A.C.P., M. González, M.D. and S. Sarita-Valdés, M.D., Depts. of Medicine and Pathology, VA Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

A female in her early 50's was in her usual health until the Fall 1975 when she developed SOB, orthopnea, cough, productive of yellow sputum and anorexia. Was seen by her physician, treated with antibiotics without improvement and referred to the University Hospital. On admission she was tachypneic and acutely ill, low grade fever was present. Physical examination was compatible with pneumonic findings, and occasional wheezes. Chest x-ray showed bilateral diffuse interstitial infiltrates. Pulmonary function studies revealed an obstructive pattern. She was given penicillin and gentamicin without improvement. Sputum, blood, urine and throat cultures grew no pathogens. CBC was normal including a WBC count of 10,700. SMA-12 was normal, PPD was negative X2. Upon review of history she denied exposure to birds, parrots, parakeets, there was no history of a similar illness in the family, nor earache. No history of exposure to TBC. During the summer of 1975 she visited Western USA and several cattle and sheep raising farms. An open lung biopsy was performed revealing an interstitial pneumonia, and small round coccobacilli on special stain compatible with rickettsiae. The diagnosis was confirmed by increase in serologic titers against Coxiella burnetti. Serologies for myeoplasma and psittacosis were negative. She was treated with tetracycline for 3 weeks with improvement and cure. We will discuss the epidemiology, diagnosis and management of the patient with atypical pneumonia.

DENGUE HEMORRHAGIC FEVER: A CASE REPORT

C. León Valiente, (Associate), C. Ramírez-Ronda, M.D., R.

H. Bermúdez, (Member), F. Pérez Rivas, M.D., R. López Correa, M.D. and B. L. Cline, M.D., VA Hospital, University of Puerto Rico School of Medicine and San Juan Laboratories-CDC, San Juan, Puerto Rico.

Dengue is endemic in PR and the Caribbean. Dengue with hemorrhagic manifestations is rare in the Western Hemisphere and not reported until recently in the Caribbean. A male in his mid 40's, in good health had the sudden onset of fever, chills, headache, generalized malaise, body aches and anorexia. He was diagnosed as a "flu" like illness and treated with analgesics and antibiotics by his physician. After 48 hrs of therapy there was no improvement, and 2 days later developed a generalized petechial rash and bleeding from the gums. He was sent to VA Hospital where he was found acutely ill with normal vital signs and low grade fever. There was a generalized petechial rash involving skin and mucuous membranes, bleeding gums, large echymosis over right shoulder and scleral icterus. There was leukopenia, thrombocytopenia, normal hemoglobin and hematocrit. Bone marrow was compatible with immune thrombocytopenia. On the second hospital day he experienced tarry stools. He was treated with corticosteroids and platelet transfusions. Clinical response was excellent in two days, corticosteroids were tappered down over a 6 week period. Diagnosis of dengue was confirmed by serologic rise against dengue 2 virus by complement fixation and hemagglutination inhibition test. Immunoglobulin and complement levels remained unaltered during the illness. We will discuss the pathogenesis, clinical presentation and management of an apparent uncommon illness, dengue with hemorrhagic manifestations.

CANDIDA TROPICALIS ARTHRITIS: A RARE ENTITY

R. Alejandro-Alejandro, M.D., E. López-Enriquez, M.D., N. Cruz, M.D., and C. Ramírez Ronda, F.A.C.P., University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

A 70-year old retired carpenter was admitted to the University Hospital with septic arthritis. *Staphylococcus epidermidis* was grown from the knee. The orthopedic surgery service performed an open drainage procedure with continuous irrigation and removed a torn meniscus. After seven days of continuous local antibiotic irrigation and systemic antibiotics the involved knee was found to be hot and swollen. The patient developed fever, antibiotics were changed to gentamicin plus methicillin. Grain stain of the joint aspirate revealed yeast cells, *Candida tropicalis* on culture. There was no evidence of dissemination. The patient was started on amphotericin B. After receiving 426 mg, therapy was stopped due to deterioration of renal function. Two days later there was a flare up of the knee. A synovial biopsy revealed yeast cells but joint fluid culture was negative for Candida. He was restarted on alternate day amphotericin B with mannitol. The knee inflammation subsided and there is no evidence for redness, tenderness or fluid accumulation. The patient is ambulating well. We want to share our experience in the treatment of fungal arthritis and to review the pathogenecity of Candida species and fungal arthritis. Specially when this is the second report of joint infection with *Candida tropicalis* in the English literature.

SERUM HEPATITIS VACCINE READY FOR HUMAN TESTS

CHICAGO – A vaccine against serum hepatitis, a liver disease sometimes transmitted in blood transfusions, has been successfully tested in animals and is now ready for human trials, says a research report in the June 28 issue of the Journal of the American Medical Association.

The vaccine is highly potent in inducing antibody formation against serum hepatitis in guinea pigs, monkeys and chimpanzees after three injected doses, says Eugene B. Buynak, Ph. D., and colleagues. The report is from the Merck Institute for Therapeutic Research, West Point, Pa.

Tests of the vaccine for control of hepatitis B (serum hepatitis) in man are to be carried out, Dr. Buynak reports. The vaccine is made from a highly purified virus by treating with formaldehyde solution, and has been tested for safety and potency, he says.

A medical text book declares that post-transfusion hepatitis is a major public health problem. It is a hazard of blood transfusion, particularly when the donors are drug addicts. Pooled plasma may be contaminated with the virus.

It may be transmitted by using inadequately sterilized syringes, hypodermic needles, dental and surgical instruments, tattoo needles, and razors, as well as through transfusions. Professional laboratory workers are subject to occupational exposure, and heroin addicts who share infected needles are a high risk.

NEW TECHNIQUE IMPROVES CURE RATE OF COLON, RECTAL CANCERS

CHICAGO – Cancer of the colon and rectum ranks second as a cause of death from cancer in the Western world, and there has been little change in the overall cure rate in the past 20 years.

Lung cancer is first among men, breast cancer among women. Colorectal cancer is second for both sexes.

In the June 28 issue of the Journal of the American Medical Association, two Long Island physicians report a marked increase in survival rate of individuals with colorectal cancer through a combination therapy of surgery and use of a potent drug, fluorouracil. Fluorouracil has been used in treating these cancers for some years. The New York doctors tired a new approach to using the drug.

The new schedule calls for using the drug four to six weeks after surgery, rather than immediately. The drug was found to be more effective when administration was delayed a few weeks, say Min C. Li, M. D., and Stuart T. Ross, M. D., of Nassau Hospital, Mineola, N. Y.

In those patients with colorectal cancer in an intermediate stage, Stage 2, the five-year rate of survival without recurrence of the disease was 58.5 per cent when treated by surgery alone, but this figure rose to 81.6 per cent with the use of the drug, say Drs. Li and Ross.

For those in a more advanced stage, Stage 3, some 24.3 per cent survived five years without evidence of disease with use of surgery alone, whereas in those combining surgery and fluorouracil the number rose to 57.5 per cent, they report.

MIND-ALTERING HERBS ARE NEW DRUGS OF ABUSE

CHICAGO – There has been a recent substantial increase in use of herbal cigarettes, teas and capsules in the United States with a consequent increase in cases of acute and highly unpleasant physical and mental reactions from these "natural and legal drugs," says a report in the Aug. 2 issue of the Journal of the American Medical Association.

The herbal products are readily available in health food stores and by mail order from suppliers and importers, says Ronald K. Siegel, Ph.D., of the UCLA School of Medicine, Los Angeles.

Many preparations contain substantial amounts of psychoactive substances, and their use has resulted in a number of intoxications requiring medical attention, Dr. Siegel says.

There are presently 193 distinct herbs commercially available as smoking substances, mostly in cigarettes. Often the cigarettes contain nonpsychoactive ingredients, such as yerba santa, rosemary, thyme, mullein and spearmint. But almost half do contain plants with known mind-altering effects, he reports.

Dr. Siegel reports on two men who experienced severe hallucinations and highly unpleasant physical and emotional reactions from smoking "Mint Bidis," hand-rolled cigarettes imported from India. Made from Indian herbs, the cigarettes were found to contain high amounts of mind-altering substances.

There are 396 herbs and spices commercially available for use as herbal teas, he says. Some 43 of these contain psychoactive substances, usually in such small amounts as to have little or no behavioral effects. However, an occasional individual will have adverse effects. One woman experienced serious unpleasant reactions after drinking a tea consisting of two ground nutmegs in a glass of warm water. She had hallucinations of monsters trying to engulf her.

Other herbal products are available as capsules, some with excessively high doses of caffine and other substances, he says.

"While the use of herbal medicines dates back to ancient Chinese and early Greek practice, nonmedical experimentation with herbal intoxicants is enjoying a recent revival as users search for legal alternatives to the ever-increasing list of restricted drugs. Most of the herbs are promoted for their apparent hallucinogenic, euphoric, or marijuana-like effects. The ready availability of these substances and their marketing in the context of 'health foods' represents a potential abuse problem," Dr. Siegel concludes.

NOTICIAS

FROM HEW NEWS

The Department of Health, Education, and Welfare published final regulations whcih set conditions for Medicare coverage of treatment for chronic kidney failurc.

The purpose of the regulations is to help beneficiaries receive appropriate care, to encourage the best use of treatment resources, and to provide the flexibility neeessary for the delivery of proper care by physicians and facilities.

Sinee July 1973, Medicare has covered virtually all people under age 65 who have permanent kidney failure when they need maintenance dialysis treatments or a kidney transplant. To be eligible for Medicare under the kidney disease provision of the law, a person must have worked long enough under social security or the railroad retirement system, or be the wife, husband, or dependent child of such a worker.

Approximately 26,600 beneficiaries will have received treatment under the program at an annual cost of $450 million during fiscal year 1976.

Under the regulations, treatment facilities are required to join together into "networks" so as to assure coordinated patient referral and access to resources. This approach permits the concentration of equipment and specially trained personnel where they can be used most effectively. The designation of network areas is the responsibility of HEW.

Each network is required to organize itself through the establishment of a Network Coordinating Council, with representatives from all treatment facilities in the network. Through its Council, each network must establish a Medical Review Board to assess patient care and service.

Survey and certification of facilities for compliance with the conditions for coverage will be performed by State health agencies in conjunction with HEW Regional Offices under the same survey and certification process now in effect for all providers and suppliers of services under Medicare. Those kidney treatment facilities not qualifying under the regulations will be phased out in such a way as to minimize any disruption of service to the patients.

To participate in the kidney treatment program, a facility must serve a minimum number of patients. This number is based upon the number of dialysis machines the facility has and the number of kidney transplants performed.

The amendments will be effective 90 days after publication in the Federal Register.

FROM AMA NEWS

ESTROGEN FOR CONTRACEPTION AND MENOPAUSE UNDER ATTACK.

CHICAGO– The use of estrogen in treating symptoms of menopause and in oral contraception is under growing attack, says a report in the Journal of the American Medical Association (Medical News Section, Feb. 23).

Oral contraceptives – the Pill – have been linked to increased risk of heart attack in young women and increased risk of breast cancer in certain groups, while estrogen therapy for menopause symptoms has been linked to increased risk of cancer of the uterus, says the JAMA report.

A British research group reported last summer that young women taking oral contraceptives are more likely to suffer heart attack. This finding was further confirmed by the report of a Stanford University group in the Feb. 23 issue of JAMA.

The link between oral contraceptive use and elevated risk of breast cancer in certain individuals was reported last fall by a California research group. The California study showed a 2.5-fold increase in breast cancer among women who had been taking oral contraceptives for a period of two to four years.

An additional risk for users of estrogens was reported in JAMA of Feb. 16 by a Kentucky research group, which found that there was increase in liver tumors among users of the Pill. Primary tumors of the liver, previously rare among women in the United States, began to occur with increasing frequency after the introduction and widespread use of the Pill, the Kentucky group declares.

Two reports last December in the New England Journal of Medicine linked an increase in cancers of the lining of the uterus to the taking of estrogens to relieve the "hot flashes" and other unpleasant symptoms of the menopause, the JAMA article declares.

The Food and Drug Administration has announced plans to draft new labeling for all estrogen products that would include strong restrictive warnings. There have been hints, says JAMA, that the sequential oral contraceptives may be removed from the market altogether unless the manufacturers can convince the FDA that there is a population for whom these preparations are advantageous. One wide-selling sequential was taken off the market in Canada in January.

LITTLE UNJUSTIFIED SURGERY IS FOUND IN NEW YORK STUDY

CHICAGO– Using a technique hailed by federal officials as "the most comprehensive assessment study in the country," a New York group found that the incidence of unjustified surgery in 12 Brooklyn-Long Island hospitals was "less than 1 percent."

The study extended over a period of several years, with the aid of other groups, and included 1,900 diagnoses and 3,800 procedures.

Each disease was analyzed by history, physical examination, services suggested where feasible, indications for surgery, preoperative preparation, operative description, pathology, and postoperative course.

Using these preset critiera predictors, the Brooklyn-Long Island chapter of the American College of Surgeons sponsored a study of surgical procedures in 12 hospitals in their area. It covered a broad mix of the surgical care in the hospitals, reviewing many of the most commonly performed operations.

By analyzing history, physical examination, laboratory data, the indications for surgery, with operative and pathologic report astthe basis, we were able to assess whether a surgical procedure was justified or unjustified and pinpoint the area of deficiency.

The incidence of unjustified appendectomies was 2.67 percent, which is below the acceptable national range and may indicate that our surgeons were too conservative. The incidence of unjustified surgery in 833 consecutive cases was less than one percent. We believe this is a more realistic percentage and refutes the myth of a 24 percent incidence of unjustified surgery being publicized in the news media.

MASSAGE OF SCALP INCREASES HAIR LOSS

CHICAGO– Vigorous scalp masage is a "no no" if you want to keep your hair, says a communication in the April 5 issue of the Journal of the American Medical Association.

Vigorous combing and brushing are bad for the hair.

"Shampoo and dry gently, and avoid scalp massage," are the watchwords in the JAMA item, written by Dr. Joseph B. Jerome of the AMA's Department of Drugs.

Neither the scalp nor the hair roots need massage, says Dr. Jerome. Vigorous scalp massage, with or without a shampoo, and regardless of whether the hair is dry, wet, or being briskly toweled dry, is mechanically damaging to the hair. Vigorous manipulation of hair, whether by massaging, shampooing, drying, brushing, or combing, tends to break hair mechanically and thus to produce characteristic artificial alopecia (the hair roots are still healthy and viable, but there is not much to show for it above the scalp), he says.

One last word: all individuals lose from 25 to 100 hairs a day. This loss is usually not noticed until an individual becomes concerned with hair loss, at which time normal hair loss is often aggravated by mechanical loss due to manipulation procedures.

WIPING OUT OF DRUG ADDICTION CALLED IMPOSSIBLE GOAL

CHICAGO– No "crusades" will wipe out narcotic addiction, and the best we can hope to do is to contain the problem, limit its scope, and offer help to the victims, says a report in the current (March) issue of Archives of General Psychiatry, a scientific journal published by the American Medical Association.

"Of course, if there were no heroin, there would be no heroin addicts – an incontrovertihle prediction, but a sterile one – since for 60 years it has proved impossible to eliminate the availability of heroin or other opiates. There is good reason to believe that it is impossible in principle (at least in a society that values individual freedoms and the right of privacy) to abolish the supply of narcotics.

The heroin addiction problem cannot be eliminated by controls over supply alone.

Since the disorder is self-inflicted and self-maintained, no treatment is possible without some positive motivation on the addict's part.

All-or-none goals in treating heroin addicts are unrealistic. If the condition of the addict's life can be improved, even though he is not cured, treatment is worthwhile.

All addicts can benefit from support of medications as a part of treatment.

Small steps are easier to accomplish than big steps, and a systematic treatment plan will proceed gradually, a little at a time.

AMA COMMISSION TO ATTACK RISING MEDICAL CARE COSTS

CHICAGO– A frontal attack on the rising cost of medical care will be launched by the new blue-ribbon National Commission on the Cost of Medical Care named this month by the American Medical Association.

The Commission has been created by the AMA to appraise factors leading to rising expenditures and to review optional courses for public and AMA policy in coping with increased costs.

Factors involved in rising costs include:

* - Greater public utilization of health care services, with the advent of Medicare, Medicaid and the growth of private health insurance;

* - Increased public expectations from medical care as an outcome of many technological advances that make possible relief or cure of conditions that were largely untreatable in the past;

* - Inflation in the economy as a whole that also is reflected in rising costs of medical care;

* - Many local, state and federal government health care programs that have broadened the availability of medical care and also have added to the cost;

* - The Commission will explore the operational aspects of the health care delivery system and will facilitate nationwide discussion and dissemination of the facts and issues regarding health care costs.

NEW RAT POISONS HELD DANGEROUS TO CHILDREN

CHICAGO – Rats have become resistent to the traditional rat poison – warfarin – and the public has turned to yellow phosphorus to control the rodents. One result is that children are being poisoned too, says a report in the March 29 issue of the Journal of the American Medical Association.

The rat poisons containing yellow phosphorus are pastes to be spread on bread or crackers and left for the rodents. But children also are attracted to these baits, researchers from the University of Texas Health Science Center at Houston Medical School report.

During the first quarter of this century, yellow phosphorus was readily available and provided source for accidental poisoning, Drs. Simon and Pickering relate. Match tips and fireworks both contained yellow phosphorus, and the chemical was used in quack remedies. Since that time, legislation and international trade agreements have eliminated it from matches, fireworks, and unscientific remedies. But it is returning as rat poison.

In an accompanying editorial in the Journal, Dr. Hugh H. Hussey, editor emeritus, points out that phosphorus is not among the top ten potentially toxic substances ingested by children. But it still is dangerous.

The top ten are, in order of frequency, aspirin, detergents and cleansers, plants, vitamins and minerals, antihistamine compounds and cold remedies, perfume and cologne, disinfectants and deodorizers, miscellaneous medications, drugs for emotional problems, and household bleach, according to the Food and Drug Administration.

CITOPATOLOGIA PARA PATOLOGOS

El *Décimo Octavo Instituto de Citopatología para Patólogos* será ofrecido en The Johns Hopkins University School of Medicine y en The Johns Hopkins Hospital, en Baltimore, Maryland, del 11 al 22 de abril de 1977.

La solicitud para participar en el Instituto debe ser enviada antes del 28 de febrero de 1977. Para mayores detalles escriba a: John K. Frost, M. D., 610 Pathology Building, The Johns Hopkins Hospital, Baltimore, Maryland, 21205, U. S. A.

FROM THE NETWORK FOR CONTINUING MEDICAL EDUCATION - Richard Christian, Director of Network Affairs, 15 Columbus Circle, New York, N. Y. 10023 (212) 541-8088

SCHEDULE OF UPCOMING PROGRAMS FOR THE NETWORK FOR CONTINUING MEDICAL EDUCATION

OCTOBER 4 - OCTOBER 17

"HIGH RISK PREGNANCY - AVOIDING SURPRISES,"

with Louis Gluck, MD, Professor of Pediatrics and Obstetrics and Director of Perinatology at the University of California Medical Center at San Diego.

"BEHAVIOR MODIFICATION: TREATMENT OR COERCION?,"

with Bernard Towers, MB, ChB, Professor of Anatomy and Pediatrics, and James Q. Simmons, III, MD, Associate Professor of Psychiatry and Chief of Child Psychiatry at the Neuropsychiatric Institute; both at the University of California at Los Angeles; and Daniel Wikler, PhD, Assistant Professor of Philosophy and Medical Ethics and Marilyn Wikler, PhD, Assistant Professor in the School of Social Work, both at the University of Wisconsin, Madison.

OCTOBER 18 - OCTOBER 31

"HYALINE MEMBRANE DISEASE: ASSESSING LUNG MATURITY,"

with Louis Gluck, MD, Professor of Pediatrics and Obstetrics, University of California San Diego, LaJolla.

"THE CLINICIAN AND THE LABORATORY: INFECTIOUS DISEASES,"

with Richard H. Parker, MD, Chief of Infectious Disease, Veterans Administration Hospital, and Associate Professor of Medicine, Howard University, Washington, D. C.

"DYSPNEA: SIGNAL OF DISEASE?,"

with Kenneth M. Moser, MD, Director of the Pulmonary Division, and Professor of Medicine, University of California, San Diego.

NOVEMBER 1 - NOVEMBER 14

"HYPERTENSIVE RETINOPATHY: FUNDUSCOPIC FEATURES,"

with Richard E. Goldberg, MD, Director, and Larry E. Magargal, MD, Co-Director, the Retinal-Vascular Unit, Wills

Eye Hospital, Philadelphia.

"LACTIC ACIDOSIS: PATHOGENESIS AND ETIOLOGY, and
"LACTIC ACIDOSIS: DIFFERENTIAL DIAGNOSIS AND TREATMENT,"

with Philip Felig, Professor and Vice Chairman, Department of Internal Medicine, and Chief, Endocrinology Section, Yale University School of Medicine and Yale-New Haven Hospital.

NOVEMBER 15 - NOVEMBER 28

"FIBEROPTIC BRONCHOSCOPY: ITS USES AND ADVANTAGES,"

with Bernard Marsh, MD, Associate Professor of Otolaryngology, The Johns Hopkins University School of Medicine and Director, Broyles Broncoscopic Clinic, Johns Hopkins Hospital, both in Baltimore, Maryland.

"ALCOHOL INGESTION: ACUTE METABOLIC SYNDROMES,"

with Philip Felig, MD, Professor and Vice-Chairman, Department of Internal Medicine and Chief, Endocrinology Section, Yale University School of Medicine and Yale-New Haven Hospital.

"CAT SCANNING: A NEW DIMENSION,"

with John R. Haaga, MD, radiologist, The Cleveland Clinic, Cleveland, Ohio.

MANY DOCTORS DROPPING MALPRACTICE INSURANCE

CHICAGO – The latest American Medical Association physician poll indicates that one out of three doctors is considering "going bare" – practicing without any malpractice insurance.

And one out of eight respondents in the poll – 13 per cent – said he or she was currently without malpractice insurance.

Results of the poll, conducted by the AMA's Center for Health Services Research and Development, appear in the June 28 issue of the Impact section of American Medical News, the AMA's weekly newspaper for physicians.

The doctors either have dropped or are considering dropping insurance because of the escalating cost of premiums – in some states now upwards of $30,000 annually for physicians in high risk specialties.

Half of the surgeons (49 per cent), 44 per cent of the obstetrician-gynecologists, and surprisingly 41 per cent of psychiatrists said they are considering dropping malpractice insurance. Pediatricians (13 per cent) were the least inclined to favor the idea.

The malpractice crisis has hit some areas of the nation with greater severity than others, the Impact report said, and this is reflected in physicians' acceptance of the non-insurance idea. Fifty-one per cent of physicians in Pacific states, including California where the professional liability problem has been acute, say they are in favor of letting insurance lapse, as compared with about 30 per cent of physicians in other states.

One out of four physicians in the Pacific and mountain states reported they had been sued for malpractice in the last three years, as against the national average of 17 percent. Physicians in the 49-65 age bracket reported greatest frequency of suits.

WORRY OVER SLEEPLESSNESS MORE HARMFUL THAN INSOMNIA ITSELF

CHICAGO – Have trouble sleeping sometimes? Most of us do.

Ordinarily it isn't a serious health problem. Worrying about insomnia often is more of a health problem than the insomnia itself.

In the Aug. 16 issue of the Journal of the American Medical Association, Sidney Cohen, M.D., of UCLA School of Medicine, Los Angeles, points out that even staying totally awake for two or three days and nights has no known harmful effects.

The newborn spends 18 hours a day sleeping. Young adults average seven to eight hours. Aging people require still less: 4.5 to 6.5 hours a day. Rare cases are known of normal people who slept only three hours a day for years, Dr. Cohen points out.

Doctors divide insomnia into three types – Difficulty in falling asleep; sleep broken by awakening several times during the night; and, early morning awakening. Say 3 a.m. and lying there worrying about one's troubles, especially forebodings about what happens to people who do not sleep enough.

One third to half of all insomniacs actually get as much sleep as those who are unconcerned about their repose, Dr. Cohen says. Sometimes the doctor will record sleep throughout the night, just to prove to the individual that he is indeed sleeping enough.

ANUNCIOS

Venta de propiedad en el Condado de los señores Fernando Pujals.

Esta residencia ofrece gran posibilidad para un grupo de médicos que interesen establecer su oficina o laboratorio en el área de Santurce. Esta localizado en la calle Manuel Rodríguez Cerra Núm. 15, Condado, Santurce, detrás del Burger King de la Avenida Ashford, tiene 1,125 mt. cuadrado de solar, casa grande de dos niveles, con cuatro habitaciones, cuatro baños, piscina y área para estacionar - precio $225,000.00. Para más información y detalles, favor de llamar a los teléfonos 725-7365, 725-8049 y 783-0575.

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Se solicitan médicos generalistas para el Dispensario Municipal de Caguas para trabajar tiempo completo o tiempo parcial, sueldo a discutirse.

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FE DE ERRATA

En la página del Contenido del mes de julio 1976 se puso por error - Volumen 68 - Enero 1976 - Número 1, cuando debió decir: Volumen 68 - Julio 1976 - Número 7.

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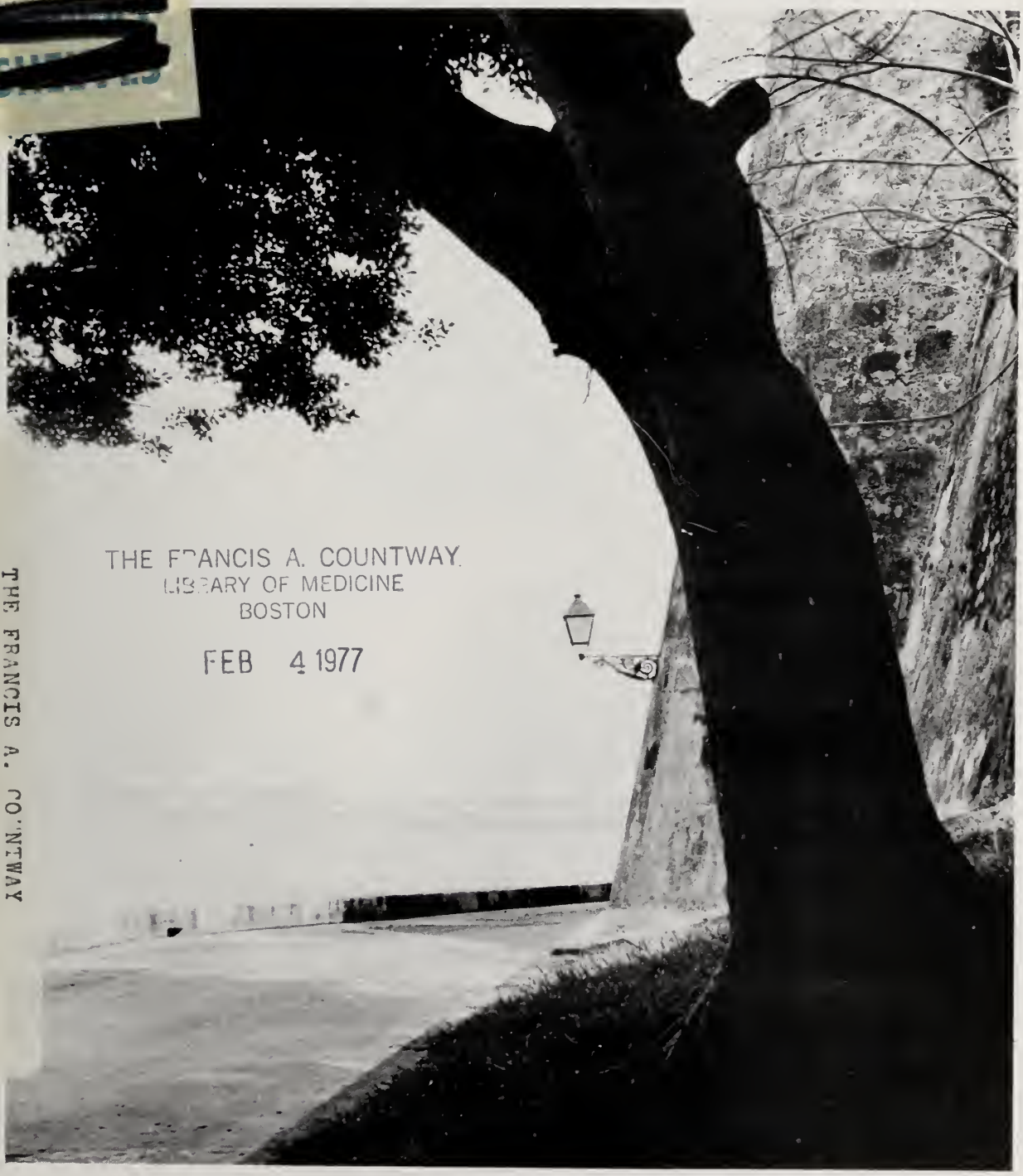


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Vol. 68 Noviembre 1976 No. 11

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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

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Valium® (diazepam) IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic anxiety states with associated depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.
If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.
Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE
Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED
Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment,* 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. *Lotion,* 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream,* 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment,* 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

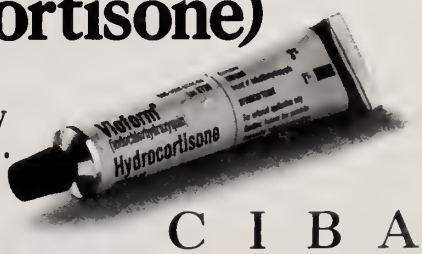
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Volumen 68 Noviembre 1976 Número 11

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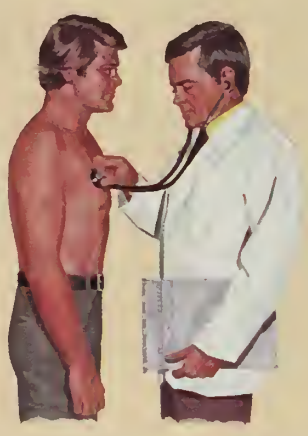
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Narrowing down pneumonias

Upjohn

Bacterial or nonbacterial?

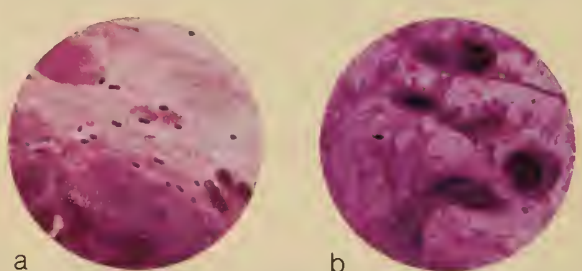
In the early stages of mild to moderate pneumonia, it is often difficult to reach an accurate bacteriologic diagnosis. A tentative differentiation may be made on history-taking, physical examination, CBC with differential analysis, and microscopic study of the sputum smear. Specimens should be obtained for culture and sensitivity testing, but when a bacterial pneumonia is diagnosed, therapy is often instituted before the etiological agent is positively identified.



Bacterial pneumonias may have a sudden onset with a shaking chill, rapid development of fever, pleuritic pain, and cough productive of rust-colored sputum. The Gram-stained sputum smear generally shows polymorphonuclear neutrophils as well as a predominance of the causative organisms. These are likely to be *Streptococcus pneumoniae*, still by far the most frequently encountered agent in bacterial pneumonia.[1] The CBC reveals marked leukocytosis with a shift to the left.

In *nonbacterial pneumonias*—mycoplasmal or viral—classical symptoms tend to develop more slowly, with myalgia, lassitude, and headache predominating. Sputum production is usually scanty, and the sputum smear is relatively uninformative, showing gram-positive cocci and other organisms which are part of the normal pharyngeal flora. The leukocyte count is normal or slightly elevated.

Direct Gram-stained sputum smears. (a) Pneumococcal pneumonia—note abundant polymorphonuclear leukocytes, as well as gram-positive diplococci. (b) Nonspecific—consistent with viral or mycoplasmal pneumonia. Note large mononuclear cell, as well as a few polymorphs and mixed bacterial flora (pharyngeal contaminants).



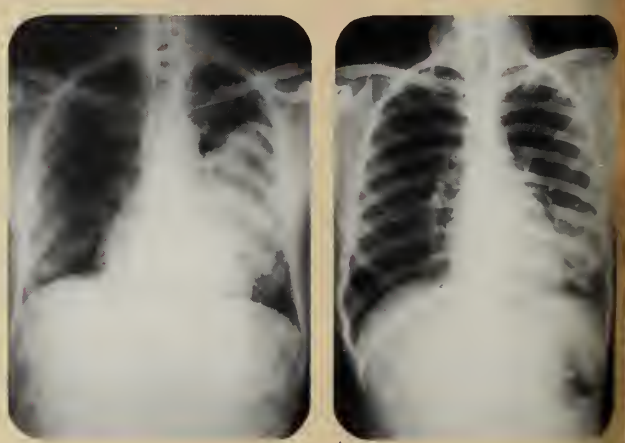
a b

Mycoplasmal or viral?

Differentiation between mycoplasmal and viral pneumonias may be impossible in the acute stage.[2]

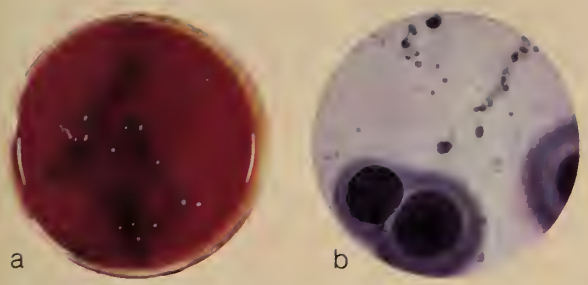
Serologic testing and culture methods for *Mycoplasma pneumoniae* are complex and time-consuming, taking as long as two weeks after obtaining samples. The sensitivity and specificity of the test for cold agglutinins have been questioned. The complement-fixing antibody test may reflect previous infection. Furthermore, facilities for culturing *M. pneumoniae* are not widely available.[3]

If treatment is to be initiated, therefore, it may be necessary to start on the basis of a *presumptive* diagnosis of mycoplasmal pneumonia.[1-3] In reaching such a diagnosis, the physician relies on clinical judgment, considering such factors as the age of the patient and the history of exposure. For example, *Mycoplasma pneumoniae* is considered the most common cause of pneumonia among ambulatory patients aged 20 to 35.[1]



a b

Chest x-rays of patients with (a) pneumococcal pneumonia—classically heavy, extensive infiltration of left lung; (b) mycoplasmal pneumonia—mild infiltrate confined to left lower lobe. Roentgenography usually does not help in differential diagnosis, since both types of pneumonias may present with a wide spectrum of x-ray as well as clinical findings.



(a) Distinct mucoid colonies of type 3 pneumococci *(Streptococcus pneumoniae)* on sheep blood agar showing greenish discoloration (alpha-hemolysis) of medium. (b) Typical "fried-egg" colonies of *Mycoplasma pneumoniae* consisting of dense central core with lighter periphery. Cultural and serologic methods for detecting *M. pneumoniae* are complex, time-consuming, and not widely available.

Expectant therapy

In the patient with a presumptive diagnosis of mycoplasmal pneumonia or bacterial pneumonia, it may be desirable to initiate antibiotic therapy before culture and sensitivity results are available.

A course of erythromycin or tetracycline is considered effective in the treatment of mycoplasmal pneumonia to help speed the clearing of infiltrate and shorten the duration of symptoms.[1,3] In pneumococcal pneumonia, erythromycin is an effective alternative to penicillin, the drug of choice. A recent report, based on data from 200 hospitals of 100 beds or more, found 98% of *S. pneumoniae* sensitive *in vitro* to erythromycin.[4]

Among these therapeutic agents, only erythromycin provides effective coverage of both *Mycoplasma pneumoniae* and *S. pneumoniae.* The penicillins are not effective against *Mycoplasma,* and *S. pneumoniae* has shown a relatively high incidence of resistance to tetracycline.

When erythromycin is selected for therapy, E-Mycin (erythromycin enteric-coated tablets, Upjohn) is a good choice. E-Mycin is administered and absorbed as active erythromycin base, and may be taken q.i.d., q 6h, or b.i.d., immediately after meals or between meals. Thus, patients can use mealtimes to help them remember their medication. The enteric coating on E-Mycin tablets helps ensure efficient absorption in the intestinal tract, and bioavailability studies show that E-Mycin can be expected to produce predictable, acceptable blood levels. The low cost of E-Mycin helps assure economical therapy.

E-Mycin rarely causes serious side effects and is not associated with liver toxicity.* The most frequent side effects are upper gastrointestinal, such as abdominal cramping and discomfort, and are dose-related. Nausea, vomiting, and diarrhea occur infrequently with usual oral doses. Serious allergic reactions, including anaphylaxis, have rarely been reported.

*Use cautiously in patients with severe liver impairment.

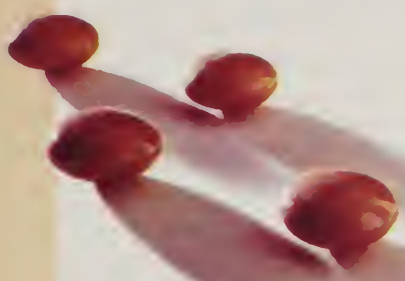
REFERENCES: 1. Chusid EL, Dalrymple W, Holloway WJ, et al: Managing the infectious pneumonias. *Patient Care* 9:122-167, 1975. 2. The occasional might of mycoplasma. *Emergency Med* 7:82, 85, 1975. 3. Stevens DA: Viral and Mycoplasma pneumonias. *Postgrad Med* 55:81-86, 1974. 4. Data source: PMR Bacteriologic Report, Winter Series 1975-1976. Data are a compilation of laboratory reports submitted during December 1975 and January and February 1976 by 200 acute care hospitals of 100 beds or more.

Summary

Because pneumonias may be difficult to differentiate at the outset, treatment is often initiated before a causal diagnosis is made. However, readily available diagnostic criteria occasionally allow early differentiation between bacterial and nonbacterial pneumonias. When the diagnosis appears to be nonbacterial pneumonia, further differentiation between mycoplasmal pneumonia and viral pneumonia is more complex and time-consuming. Therefore, therapy is often initiated on the basis of a *presumptive* diagnosis of mycoplasmal pneumonia.

Erythromycin is an effective antibiotic against *Mycoplasma pneumoniae, Streptococcus pneumoniae,*† and *Streptococcus pyogenes.*† E-Mycin (erythromycin enteric-coated tablets, Upjohn) is administered and well absorbed as the active base, may be taken immediately after meals or between meals, and is essentially nontoxic.

†Although penicillin remains the drug of choice against these organisms, erythromycin is an effective alternative.



E-Mycin® 250 mg

erythromycin enteric-coated tablets, Upjohn

wide-ranging usefulness in pneumonia*

*Mild to moderately severe, due to susceptible organisms.

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Please turn page for brief summary of prescribing information.

Wide-ranging usefulness in pneumonia*

E-Mycin® 250 mg

erythromycin enteric-coated tablets, Upjohn

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- For mild to moderately severe infections due to susceptible organisms that commonly invade the respiratory tract
- Essentially nontoxic (see Precautions and Adverse Reactions below)
- Documented bioavailability
- May be taken immediately after meals or between meals
- Active base formula produces predictable blood levels
- Formulated for quality...priced for economy

E-MYCIN® TABLETS — 250 mg — For Oral Administration (erythromycin enteric-coated tablets, Upjohn)
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Indications: *Streptococcus pyogenes (group A beta-hemolytic streptococci):* Upper and lower respiratory tract, skin, and soft-tissue infections of mild to moderate severity. Parenteral benzathine penicillin G is considered by the American Heart Association to be the drug of choice in the treatment and prevention of streptococcal pharyngitis and in long-term prophylaxis of rheumatic fever. When oral medication is necessary (because the parenteral route is contraindicated) or if there is known allergy to penicillin, the following recommendations made by the American Heart Association apply: 1) Oral penicillin G or V (where no allergy exists)—This is the drug of choice. Give for a minimum of 10 days; 2) Erythromycin—Give for a minimum of 10 days. A few strains of streptococci resistant to erythromycin have been reported.
Alpha-hemolytic streptococci (viridans group): Short-term prophylaxis against bacterial endocarditis prior to dental or other operative procedures in patients with a history of rheumatic fever or congenital heart disease who are hypersensitive to penicillin. (Erythromycin is not suitable prior to genitourinary surgery where the organisms likely to lead to bacteremia are gram-negative bacilli or the enterococcus group of streptococci.)
Staphylococcus aureus: Acute infections of skin and soft tissue of mild to moderate severity. Resistance may develop during treatment.
Diplococcus pneumoniae: Upper respiratory tract infections (eg, otitis media, pharyngitis) and lower respiratory tract infections (eg, pneumonia) of mild to moderate degree.
Mycoplasma pneumoniae (Eaton agent, PPLO): In the treatment of primary atypical pneumonia, when due to this organism.
Treponema pallidum: Infections due to this organism.
Corynebacterium diphtheriae and *Corynebacterium minutissimum:* As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers. In the treatment of erythrasma.
Entamoeba histolytica: In the treatment of intestinal amebiasis only. Extraenteric amebiasis requires treatment with other agents.
Listeria monocytogenes: Infections due to this organism.

Contraindication: Contraindicated in patients with known hypersensitivity to erythromycin.

Warning: Safety for use in pregnancy has not been established.

Precautions: Erythromycin is principally excreted by the liver. Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. Surgical procedures should be performed when indicated.

Adverse reactions: The most frequent side effects of erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose-related. Nausea, vomiting, and diarrhea occur infrequently with usual oral doses. During prolonged or repeated therapy, there is a possibility of overgrowth of nonsusceptible bacteria or fungi. If such infections occur, the drug should be discontinued and appropriate therapy instituted. Mild allergic reactions such as urticaria and other skin rashes have occurred. Serious allergic reactions, including anaphylaxis, have been reported.

Treatment of overdosage: The drug is virtually nontoxic, though some individuals may exhibit gastric intolerance to even therapeutic amounts. Allergic reactions associated with acute overdosage should be handled in the usual manner—that is, by the administration of adrenalin, corticosteroids, and antihistamines as indicated and the prompt elimination of unabsorbed drug, in addition to all needed supportive measures.

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*Mild to moderately severe, due to susceptible organisms

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Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

> ***Usage in Pregnancy:*** **Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

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EPITHELIAL ODONTOGENIC TUMORS

Enrique Pantoja, MD
José Enrique Ibañez, MD
José E. Taveras, MD
Ismael Rodríguez Ibañez, MD

Although the earliest odontogenic tumors on record may be the 'liquid tumors of the jaws' (cystic lesions possibly of dental origin) described by Scultet in the seventeenth century (1), and Broca in 1868 segregated the tumors of tooth germ origin under the term odontome (2), a rational classification of these lesions was not possible until the elucidation of the mechanism of normal tooth development. The reciprocal induction theory of odontogenesis, on which such a classification is now based, had its origin in the observation made by Tomes one hundred years ago that there is an enamel organ in the armadillo, though its teeth contain dentin but no enamel (3).

Similar observations in rodents led von Brunn to postulate in 1891 that the epithelial sheath (enamel organ) is essential to the formation of odontoblasts and dentin (4). Transplantation and in vitro studies with tooth germs performed in the nineteen-thirties fully supported this belief (5, 6). It was also found that not only are the ameloblasts instrumental in inducing the mesenchyme to form odontoblasts, but the production of dentin by these odontoblasts is in turn a prerequisite for the ameloblasts to secrete enamel (7). This so-called reciprocal induction theory forms the basis of the modern classification of odontogenic tumors.

The most common of these tumors, now called ameloblastoma, was first accurately described from the clinical point of view by Cusack in 1827 (8). With the advent of cellular pathology in the mid-nineteenth century, the existence of these epithelial tumors within the confines of the jawbones became a histogenetic mystery, finally resolved by Malassez in 1885 when he recognized the existence of epithelial remnants of the enamel organ in the jaws of normal adults (9). These 'debris épithéliaux paradentaires', as he called them, could give rise to a tumor of the jawbones which he called adamantinoma.

This term, indiscriminately used at first to include tumors which contained both mesenchymal and epithelial components, was later restricted to purely epithelial tumors in which no mesenchymal derivatives were found. In conformity with the reciprocal induction theory, this purely epithelial tumor is incapable of forming hard dental tissues (dentin, enamel and cementum), thus, the term adamantinoma, which etymologically means hard tumor, is a misnomer. The name ameloblastoma, from amel (old French word meaning enamel) and the Greek word blastos (germ) (10), introduced by Churchill (11) in 1934, has been uniformly adopted in the English medical literature. The group of epithelial odontogenic tumors now includes, in addition to ameloblastoma, the calcifying epithelial odontogenic tumor of Pindborg, adenoameloblastoma, plus the mixed (epithelial and mesenchymal) ameloblastic odontoma, ameloblastic fibroma and ameloblastosarcoma.

Discussion

Our personal experience with these tumors is based on eight cases, the clinical features of which are summarized in Table I. Seven of these cases were ameloblastoma, six of which originated in the mandible, the most common location. There was one maxillary ameloblastoma presenting as a primary antral lesion, and one ameloblastic odontoma originating in the mandibular incisor region of a four year old boy.

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TABLE I
CLINICAL DATA IN 8 PATIENTS WITH EPITHELIAL ODONTOGENIC TUMORS

	Age	Sex	Symptoms	Onset (Yr)	Histology	Operation	Survival (Yrs)	Remarks
1	45	F	Painless swelling	1935	Ameloblastoma	Segmental resection 11-23-48	6	No recurrence. Died of uterine cancer 12-16-54.
2	60	F	Huge mass	1949	Acanthotic ameloblastoma	Hemimandibulectomy 3-1-54	10	No recurrence. Died of cancer of the esophagus.
3	36	F	Ulcerated mass	1934	Malignant ameloblastoma	2/3 of mandible resected 3-31-52.	16	Malignant histologic features. No recurrence.
4	48	F	Pain & swelling	1967	Cystic ameloblastoma	Partial mandibulectomy 2-27-69	6	Living free of tumor.
5	35	F	Painless mass	1948	Ameloblastoma	Hemimandibulectomy 12-9-50.	18	No recurrence 18 years after surgery.
6	35	M	Painless mass	1945	Acanthotic ameloblastoma	Curetted 8-27-51. Resected 7-9-58.	17	Recurrence after curettage. No recurrence 17 yrs. after resection.
7	65	M	Painful mass	1974	Ameloblastoma	Palliative radiotherapy	1	Inoperable antral lesion. Pain responded to radiotherapy.
8	4	M	Painless	1969	Ameloblastic odontoma	Curettage	6	Cured by curettage.



Fig. 1-A: *Large ulcerated ameloblastoma in a 36 year old woman. B) Patient three years after extensive resection of mandible.*

Ameloblastoma

This is the most common odontogenic tumor, though it represents only 1 percent of all cysts and tumors of the jaws (12). It usually occurs in adults before the age of 40, has a peak incidence at 37, and is rare at both extremes of life. Both sexes and all races and nationalities are equally affected, the lower jaw being the site of the tumor in 80 percent of the cases. It has also been reported in fish and in many domestic animals (13).

This tumor grows slowly, producing a gradual swelling of the affected jaw which may cause marked facial deformity, and may ulcerate (Fig. 1), resulting in a chronic draining sinus in up to 28 percent of the cases. Though it is rarely painful, the tumor may obstruct the airway, interfere with nutrition or erode a major blood vessel causing a fatal hemorrhage (14). Invading the facial bones and the base of the skull, it may extend into the cranial cavity, involve the brain and end fatally (15).

If adequately excised, ameloblastomas are curable even when locally advanced (Figs. 1 A & B). The neglected or improperly treated tumor, however, may become locally infiltrative and difficult to eradicate. It may occasionally become frankly malignant, producing distant metastases, usually to the lymph nodes (16, 17), bones (12, 18) or lungs (15, 17). Lymphatic metastases are the most common, but hematogenous spread may also occur as demonstrated by the detection of tumor cells in the pterygoid venous plexus (17) and in the pulmonary vessels (19). More rarely, spread may occur to the lungs via the bronchial tree. Aspirated tumor cells have been found forming a cast of the bronchial lumen, growing in it, causing bronchiectasis and invading the surrounding lung parenchyma (20).

When the tumor arises in the maxilla it tends to



Fig. 2: *Maxillary ameloblastoma presenting as an antral lesion with destruction of middle and superior walls of the antrum.*



Fig. 3: *Mandibular ameloblastoma showing a multilocular radiolucent defect on x-rays.*

invade the antrum (Fig. 2) or nasal passages, resulting in obstruction of these passages, rhinorrhea, or epistaxis (21). The eye may be involved, causing proptosis and visual symptoms, or the tumor may grow into the oral cavity pushing the palate down and inverting the palatal arch. The molar region is the most frequent site of origin in both maxilla and mandible, and the initial symptoms may be related to the teeth - loosening of the affected molars, tooth aches, numbness or dental malocclusion (22). The tumor may sometimes become infected and may simulate a periodontal abscess; it may be associated with facial cellulitis. The infection may become chronic and pus may drain for years into the oral cavity (23), or through a cutaneous fistula to the outside.

By radiographic means it is now possible to detect this tumor while still asymptomatic (Fig. 3), and many cases are being discovered accidentally on routine dental films. The tumor presents as a unilocular or multilocular radiolucent defect, without calcifications or radio-opaque dental tissues. The margins of the defect are sharp; the adjoining bone appears intact, although the cortex may be expanded. The appearance is that of a non-infiltrating, expansile, centrally placed tumor, lacking the 'moth eaten' type of bone destruction characteristic of malignant tumors.

If the ameloblastoma has originated within a follicular cyst, which is not rare (24, 25, 26), the radiographic findings are those of the pre-existing cyst. In this case the defect is unilocular and its margins are not only sharp, but contain unusually dense bone - the so-called sclerotic margin characteristic of a benign cyst. Cystic degeneration is also frequent in the initially solid ameloblastoma, and these cysts may contribute to the multilocular 'soap bubble' radiographic appearance of most of these tumors. The cystic component may be so inconspicuous as to be seen only on section of the tumor or on microscopic examination.

Ameloblastoma has a variable, but generally characteristic microscopic appearance, most tumors presenting either a follicular or plexiform pattern (27). In the former the ameloblasts are aggregated in epithelial islands set in a collagenous stroma (Fig. 4). The periphery of the islands is lined by a row of columnar cells in a palisade arrangement, with the nuclei polarized away from the basement membrane surrounding each island (25). Next to the palisade of ameloblasts there is a transition zone corresponding to the stratum intermedium of normal odontogenesis, and the central



Fig. 4: *Follicular type of ameloblastoma.*

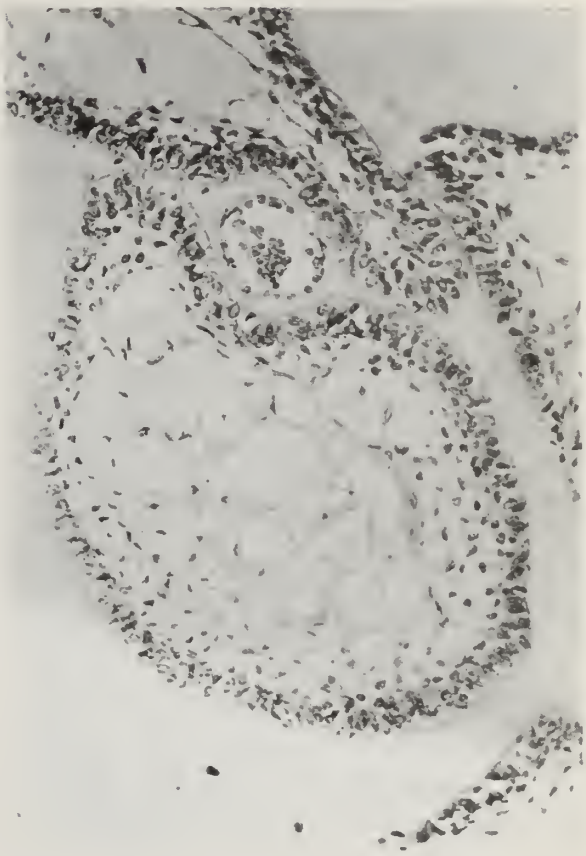


Fig. 5: *Epithelial island with early cystic degeneration of stellate reticulum. Note distinct basement membrane with polarization of nuclei away from it.*

portion of each island is occupied by loosely arranged, stellate-shaped cells, the equivalent of the stellate reticulum of normal tooth development (Fig. 5). The stellate reticulum cells of ameloblastoma occasionally become granular cells (28, 29), or they may undergo squamous metaplasia (Fig. 6); more often the cells simply degenerate, disappear, and the central portion of the epithelial islands becomes the site of tiny cystic cavities (Fig. 7). In time these cavities may coalesce, resulting in the formation of a grossly cystic tumor.

The other common histologic pattern seen in ameloblastoma is called plexiform because the ameloblasts are arranged in branching or interconnecting strands instead of discrete islands. The formation of a stellate reticulum within the epithelial strands is rare, but as in the follicular pattern, the strands lie in a collagenous matrix. Occasionally, anaplastic and pleomorphic ameloblasts may occur in some lesions (Fig. 8), however, the histologic findings do not correlate well with clinical behavior and should not dictate the approach to treatment.

The treatment of choice for this tumor is adequate resection. The small, early mandibular lesion may be amenable to a conservative excision which spares the continuity of the mandible, or to a combination of curettage and cauterization (30) or cryotherapy (31). Most mandibular lesions, however, and all the maxillary ones require at least a partial resection of the involved bone. Occasionally, a more radical procedure is necessary to insure complete resection of the tumor (Figs. 1 A & B). With adequate initial resection the prognosis is good for both mandibular and maxillary ameloblastoma. Recurrences in the mandible may still be amenable to radical surgery, but maxillary recurrences are usually incurable (32), which puts a premium on the adequacy of initial resection for maxillary ameloblastoma.

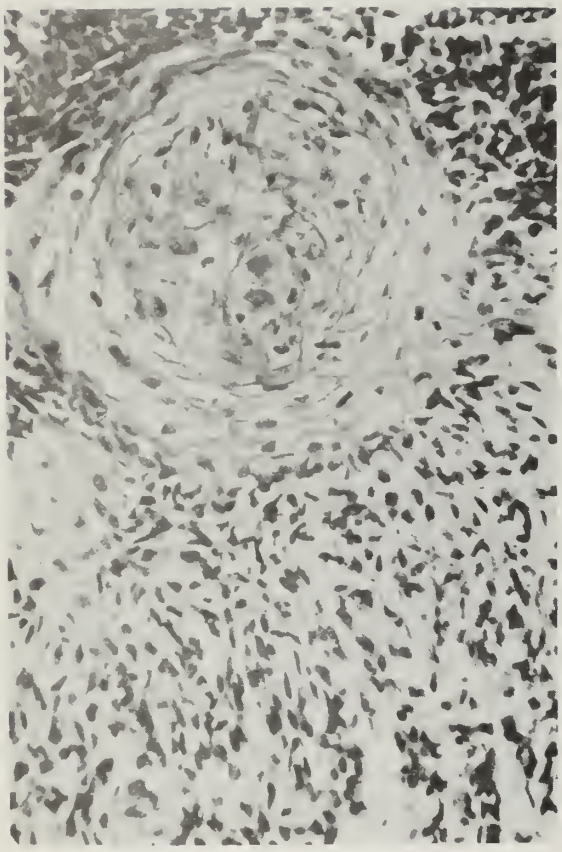


Fig. 6: *Area of squamous metaplasia surrounded by atypical ameloblasts in maxillary ameloblastoma.*



Fig. 7: *Mandibular ameloblastoma showing microcystic degeneration of stellate reticulum. Note long rows of columnar ameloblasts with distinct basement membranes. Arrows point to microcysts.*

Other purely epithelial neoplasma

Of the purely epithelial odontogenic tumors, none resembles ameloblastoma so much regarding age incidence and clinical behavior as does the tumor described by Pindborg in 1958 as 'calcifying epithelial odontogenic tumor' (33). This lesion affects mostly adult males under forty, originates in the premolar region, especially in the mandible, and is often associated with an embedded tooth. Its most outstanding feature is the presence of multiple, rounded, dense calcium deposits which may be so abundant (particularly in old tumors) as to cast a radioopaque image of the lesion on x-rays. In most cases the radiographic appearance combines radiolucent and radioopaque densities.

Due to its purely epithelial nature the tumor does not form hard dental tissues. The calcium is deposited in degenerated cells in the form of spherical concretions which may be found among the epithelial cells or in the connective tissue stroma. The tumor cells are large, polyhedral in shape, contain abundant cytoplasm and are separated by a scanty stroma (34). Like ameloblastoma, this tumor is locally aggressive and has a tendency to recur if incompletely resected.

The lesion generally known as adenoameloblastoma (glandular ameloblastoma or ameloblastic adenomatoid tumor) is another purely epithelial lesion of tooth germ origin. It is characterized histologically by the presence of duct-like structures lined by a single layer of medium to tall columnar cells. The 'ducts' may contain hyalin material, or their walls may be compressed into 'potential tubules' obliterating the lumen (34). Calcified material may be seen within the lumen or scattered

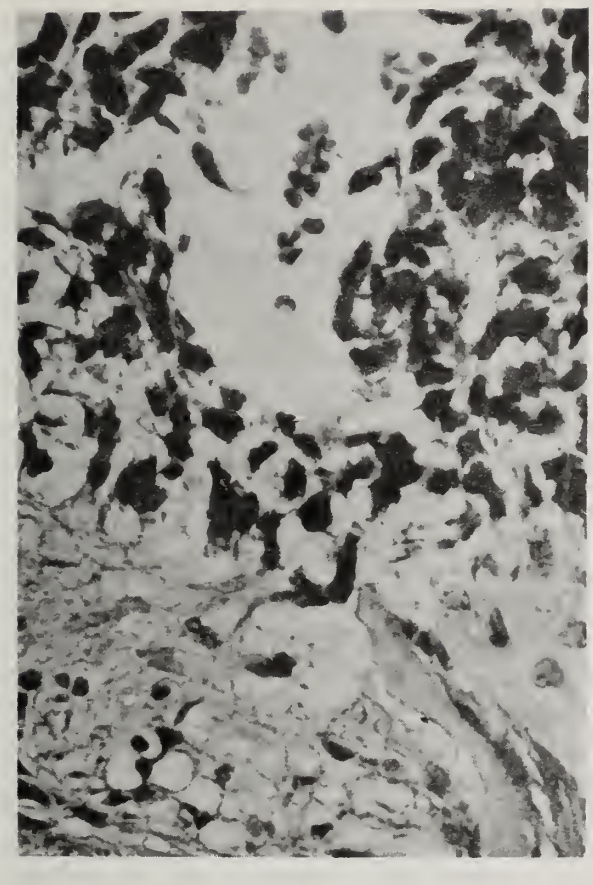


Fig. 8: *Bony trabecula (lower right of picture) surrounded by poorly differentiated ameloblastoma.*

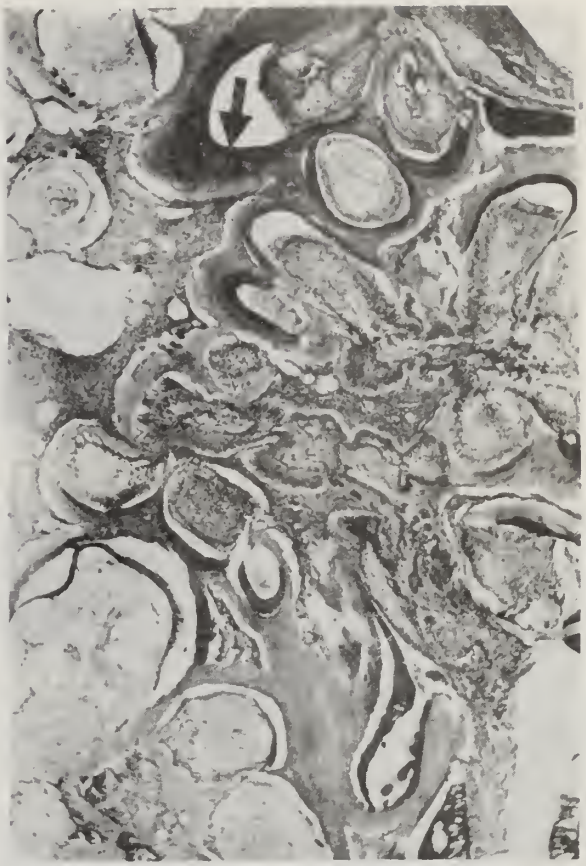


Fig. 9: *Classic microscopic features of ameloblastic odontoma. Arrow points to one of many semilunar, dark-staining 'enamel crowns'. The ameloblasts, however, are on the inside (partly receding away from) the secreted enamel. The lighter-staining dentin surrounds the 'enamel crowns', the opposite of normal odontogenesis. Poorly formed denticles results.*

throughout the epithelial tissue. This calcification, however, is not enough to show radiographically; the lesion presents a purely radiolucent image like ameloblastoma. Unlike the latter, adenoameloblastoma occurs primarily in the maxilla, and mostly in females during the second decade of life. It expands the bone, but is noninvasive; it 'shells out' easily, and does not recur even after conservative curettage.

Mixed epithelial and mesodermal tumors

These include ameloblastic fibroma, ameloblastic odontoma, and their malignant counterparts, ameloblastosarcoma and ameloblastic odontosarcoma. Most cases of ameloblastic fibroma occur between the ages of five and twenty years and this lesion is responsible for some of the ameloblastomas reported in children. It may resemble the latter lesion both radiographically and microscopically. On x-rays it shows a cyst-like radiolucency which expands the bone without invading it, and the lesion may be associated with an unerupted tooth.

Histologically the ameloblastic fibroma is characterized by the proliferation of both epithelial and mesenchymal elements. The epithelial elements are arranged in cords or islands not unlike those of ameloblastoma. The stroma, however, is not made of mature fibrous connective tissue, but of rather primitive mesenchymal tissue which may be highly cellular and may have atypical features suggestive of sarcoma (34). The tumor, however, is usually encapsulated, noninfiltrating and benign.

Very rarely, a tumor, which may originate from the benign lesion, displays a frankly sarcomatous stroma



Fig. 10-A: *Radiograph of mandible of a 4 year old boy (case 8) with ameloblastic odontoma of incisor region. Note the radioopacity of the lesion (arrows) due to the large number of calcified denticles within it. B) The patient five years later showing no evidence of recurrence. C) Radiograph at age nine showing complete repair of the mandibular defect. Note missing right lower incisors.*

without malignant change in the epithelial component - the so-called ameloblastosarcoma (35). In the few reported cases pain has often preceded the swelling and the radiographs have shown extensive, poorly defined bone destruction, two important criteria in differentiating this from the benign lesion. In addition, a high mitotic activity and the presence of abnormal mitoses also characterize the ameloblastosarcoma (35).

Some authors (36) believe that the evolution of odontogenic tumors match tooth development to the extent that an ameloblastic fibroma may proceed to develop odontoblasts, dentin and enamel, and thus become an odontoma (a tumor composed of these hard dental tissues, often with pulp and cementum as well). In normal tooth development the enamel organ lasts but a short time after the formation of the enamel crown; during this brief interval epithelium and hard dental tissues co-exist. Ameloblastic odontoma corresponds to this brief episode in tooth development, which may be why the tumor is so rare.

This lesion contains enamel epithelium and its derivatives (stratum intermedium and stellate reticulum) in association with all the structures found in the normal tooth (37, 38), (Fig. 9). The dental substances may be organized into more or less well-formed denticles which contribute to give the lesion a partially radioopaque density on x-rays (39, 40) (Fig. 10A). The periphery of the tumor, however, is marked by a radiolucent zone and the margins of the defect in the bone are well outlined (41, 42). Since the tumor grows very slowly and is virtually asymptomatic, it is often detected accidentally on routine dental radiographs (36). Most of these lesions are discovered during the first two decades of life (40), are well encapsulated (43), can be easily enucleated, or may be cured by conservative curettage (44) (Figs. 10 B & C). They hardly ever recur (45).

The extremely rare ameloblastic odontosarcoma (35, 46), on the other hand, tends to recur, is locally aggressive, and may prove fatal. Some authors do not distinguish between this lesion and the ameloblastosarcoma (47).

Summary

Three of the epithelial odontogenic tumors are purely ameloblastic: ameloblastoma (by far the most

common), the calcifying epithelial odontogenic tumor and adenoameloblastoma. The first two are aggressive tumors of adults under age 40 and may be considered locally malignant; the adenoameloblastoma is benign and occurs in the second decade of life. The two mixed (epithelial and mesenchymal) odontogenic tumors, ameloblastic fibroma and ameloblastic odontoma, are also benign and occur before age twenty. Sarcomatous degeneration of these two lesions is very rare.

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(Remaining references will be submitted upon request to the author)

VALUE OF THE SWAN-GANZ BALLOON CATHETHER IN THE DIAGNOSIS OF TRANSPOSITION OF THE GREAT ARTERIES IN AN ADULT

Charles D. Johnson, MD

The difficulty or impossibility of entering the pulmonary artery (PA) during catheterization of patients with transposition (TGA) has been appreciated, particularly in those cases lacking an atrial (ASD) or ventricular septal defect (VSD) (1-3). Catheterization of the PA in these patients is quite important in order to determine oxygen content and saturation, pressure, resistance and flow, to determine the existence of any pulmonary valvular or subvalvular stenosis (PS), and to assess the adequacy of a previous PA banding. Pulmonary hypertension and vascular disease often complicate the course of transposition patients at an early age (about 1-2 years), precluding surgical repair (4-8). Thus, in the pre-surgical evaluation a knowledge of these parameters is a necessity (9-18).

In recent years, the flow-directed, balloon-tipped, double-lumen Swan-Ganz catheter (Edwards Laboratories - Santa Ana, California), has proven valuable in obtaining this critical information, particularly in infants and children (2, 19-23). This report confirms this previous experience, in an adult patient.

Case Report

This 26 year-old female was born cyanotic and there was difficulty in reviving her at birth; a heart murmur was detected. Her development was slow; dizzy spells, squatting and finger clubbing ensued. Cyanosis increased; dyspnea, orthopnea, easy fatigability, leg edema and frequent infections occurred. She underwent cardiac catheterizations at ages of 3 and 9 years, the results of which are unknown. A third catheterization (right median antecubital vein) was done in 1968 at the age of 19 years. The aorta (Ao) was entered from the right ventricle (RV), but the PA was not entered. The RV pressure was 102/10 mm Hg, with an oxygen (O_2) saturation of 77 percent. The aortic pressure was 96/74, mean 84 mm Hg, and saturation was 76 percent. The Ao and PA filled from the RV injection; the aortic filling was direct and dense. A VSD was present, and the PA was large. The most probable diagnosis then was double-outlet right ventricle (Taussig--Bing Syndrome), and the Cardiac Board decision was to band the PA. This was never done as the patient did not return for follow-up. Subsequently, further symptoms were noted, along with fever and petechiae. Hemoglobin (Hb) was 20.5 grams. Phlebotomies were performed.

The patient returned to our Cardiac Clinic in 1975, complaining of dyspnea, palpitations, orthopnea, easy fatigability, dizziness, headaches and "colds". She had managed to finish the fourth year of high school. She appeared frail, chronically ill and demonstrated marked cyanosis and clubbing, with scoliosis. Inspiratory coarse rhonchi were heard. Biventricular accessibility, a precordial systolic thrill, an occasional premature ventricular contraction, a single increased S_2 over the left precordium, and a grade IV ejection systolic murmur along the left sternal border were detected. The electrocardiogram and vectorcardiogram showed marked RV hypertrophy, combined atrial enlargement, a few premature ventricular contractions, a QRS complex in lead V_6, and a horizontal loop suggesting the left ventricular pressure to be greater than two-thirds of the RV pressure, with left ventricular (LV) hypertrophy usually associated with a VSD. Chamber analysis demonstrated cardiomegaly (RV, ? LV), a left aortic arch, massively increased pulmonary flow, a left-sided stomach bubble and dextroscoliosis. The Hb was 22.9 grams, the hematocrit 71 percent and red blood cell count 8.4 million.

A fourth cardiac catheterization was undertaken (left arm). The LV was entered from the right side, venous, (VSD), and was located on the left side; the RV appeared to be on the right side perhaps overlying the LV. The Ao arose from the RV, both anteriorly, the PA arose posteriorly and completely from the posterior LV and showed slight narrowing near its origin, but the main PA, right and left branches were huge. There was minimal mitral regurgitation, but no aortic-mitral continuity. The RV pressure was 88/7 mm Hg and the aortic pressure was 91/62, mean 78, and saturation of 76 percent. The LV was entered on multiple occasions - pressure here was 94/9 mm Hg, with saturation of 96 and ? 90 percent. Again, in spite of great effort, the PA could not be entered with the catheter (NIH). A week later we made a fifth attempt. Femo-

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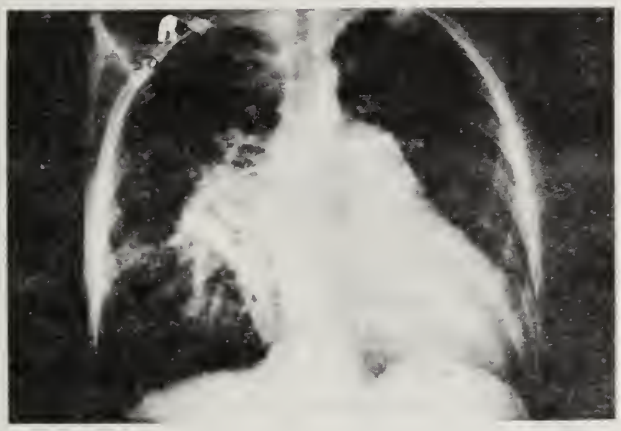


Figure 1: *Seriography, Posterio-anterior view. Manual injection into the right PA. Course of the Swan-Ganz catheter: Femoral vein, inferior vena cava, RA, RV, across the VSD, LV, main PA, right PA (Abbreviations in text).*

ral retrograde aortic catheters (Gensini, Cordis), and subsequently with a terminal curve (as suggested by Mullins) (24) entered the LV but could not be made to enter the PA. Finally, using the Desilets-Hoffman Sheath, percutaneous technique (25), and under fluoroscopic control, we passed a retrograde femoral venous Swan-Ganz balloon catheter to the RV, and through the VSD to the LV cavity. On entering the femoral vein, bradycardia and a fall in blood pressure occurred. These responded in a few minutes to atropine and time, and were probably due to the insertion of a relatively large catheter into the vein of a relatively small adult, and a vagal-type reaction. While in the LV the balloon was inflated with 1 cc of sterile CO_2; after making a few bobbing movements in the LV cavity and within one-half minute, the catheter floated superiorly to the PA! See Figure 1 for the location in the right PA with the balloon deflated. The main PA pressure was 62/22, mean 38 mm Hg, and the O_2 saturations were 96 and 98 percent in the right and left PA's.

The diagnoses are believed to be Cyanotic Congenital Heart Disease, Complete TGA (D-Loop, d-transposition; S, D, D), VSD, probable mild PS, minimal mitral regurgitation and moderate pulmonary hypertension. With this information we have decided on surgical therapy in this complex case.

Discussion

Negotiating the PA with a catheter may offer a Herculean task in patients with TGA. Cardiovascular hemodynamics are complicated in view of the separate systemic and pulmonary parallel circuits of blood flow and the mandatory presence of one or more variable and bidirectional shunts (4, 5, 7). The early onslaught of pulmonary hypertension may forbid a surgical approach in management (6, 9-18).

Catheter Methods Employed to Enter the Pulmonary Artery in Complete Transposition of the Great Arteries

Using conventional catheter techniques early attempts to reach the PA were successful in only 20-46 percent of cases (1, 26) - about 30-62 percent success if a VSD were present. Thus failures were experienced even in the presence of an ASD or VSD. The VSD, pulmonary and subpulmonary stenosis and the posterior PA arising from the posterior LV all may create obstacles and sharpe turns in the catheter course. In view of these results and the mortality (5.5 percent) associated with percutaneous LV puncture, Rahimtoola and associates in 1966 employed a modification of Radner's percutaneous suprasternal puncture technique in 23 patients, ages 1 1/2 - 19 years (1). Their method, however, was traumatic and required general anesthesia. Other special techniques have been tried. Carr and Wells used a fine coaxial flow-guided catheter in 18 children, entering via the left atrium (LA) or a VSD, with good success except in 2 patients with PS (27). A looped floppy guide or J wire via a patent foramen ovale (PFO) or ASD proved successful, safe and rapid in 7 of 9 patients, ages 6 weeks to 4 years (28).

Pickering et al. recommend a new technique which is as follows: The LV outflow tract is studied; a No. 6 Lehman catheter is passed to the LV, through which a guide wire is passed; the catheter is then removed leaving the guide in the LV; a Formocath catheter (made from Hanafee tubing and with a curve) is then passed over the guide; the guide wire is withdrawn allowing the Formocath to curve toward the PA; the guide wire (soft end) is reinserted and passed around the catheter curve and on into the PA; the catheter is advanced into the PA over the guide; the guide wire is then removed; a good quality trace can be obtained. Tynan took advantage of a catheter tip deflector (2),

Although special techniques and passage of a prograde venous catheter via an interatrial communication, LA and LV or via the RV and a VSD may allow PA entry at times, these methods may fail, may be difficult and time-consuming, especially with PS or l-transposition or with the absence of an ASD. So in 1972 Mullins and associates recommended retrograde femoral artery

catheterization by the percutaneous sheath technique, and had found it to be safe, rapid and effective in 10 patients with TGA (d and l) and VSD; ages were 10 months to 13 years. A catheter loop is preferably formed while in the aortic root, or in the systemic ventricular cavity; the catheter is then advanced across the septal defect and hooked into the PA. The average time from introduction of the catheter to destination was 10.5 minutes (24). However, the loop may get trapped under the mitral valve.

Macartney and colleagues have proven a new preformed, semirigid polyethylene catheter with a long S-bend and built-in torque control in 17 patients, ages 2 days to 6 years, entering via the saphenous, femoral or axillary vein; they recommend it on the basis that pressures, oximetry, access to other heart chambers and vessels and angiocardiography could all be realized with the same catheter; the availability of angiography was an advantage over most other catheters; passage is not dependent upon blood flow; time to destination was 40 seconds to 15 minutes (median 5 minutes). However, as this method depends upon an interatrial communication, the authors used a Shirey transvalvular catheter in 2 patients (ages 5 and 13 years) with an intact atrial septum, but with VSD's. Entry was retrograde from the axillary artery, through the aortic valve and by keeping the tip posteriorly, through the VSD and after looping and advancing in the LV, the tip passed into the PA with ease. Their failure rate with the original Cordis Cobra catheter was 20 percent (3).

Thus, different types and configurations of catheters and routes of entry-vein, artery, femoral area, arm (right and left) may be utilized; a patent ductus arteriosus might allow passage of the catheter from the Ao to the PA.

In 1970, Swan and associates predicted that their balloon-tipped, flow-guided catheter might prove valuable in the catheterization of complex cardiac malformations (20). Their predictions have been proven true in subsequent years by Kelly (21), Black (22), Stanger (23) and Jones (2) in some 60 neonates, infants and children with various types of TGA, some with PS or subvalvular PS. The PA was usually entered from the LV via a PFO, an ASD or atrial septostomy, although entry from the RV across a VSD was also accomplished (2). Thirteen patients had had a previous Mustard operation. The success rate was high although there were a few failures. Success was realized in a 12 year-old boy with TGA, VSD, PS and a venous anomaly in whom five previous studies had failed (21). This method was rapid (4.4 minutes in one study) and safe (only premature ventricular contractions and balloon rupture have occurred).

Complications

Knotting of the catheter, heart block, ventricular arrythmias and fibrillation, thromboses, PA perforation and thrombosis, venous air embolism and pulmonary complications, such as pulmonary ischemic lesions, have been observed with the use of the Swan-Ganz catheter in PA monitoring (30, 31).

The Catheter and Techniques

This catherer is soft and radiopaque, and is passed with fluoroscopic guidance. A distal molded curve may augment the success rate (2). The balloon is filled with sterile CO_2 to avoid air embolism in case of its rupture; liquid and contrast material are not recommended. The balloon is deflated once the PA is reached. Cardiogreen dye may be injected and sampled. Although angiocardiography with pressure injection is stated to be disappointing and not recommended with this catheter, it has been used for wedge angiography and we made a satisfactory manual injection through it. A disruption of the intraluminal septum by a pressure injection is feared. A balloon angiography catheter is now also available (19). The catheter may be introduced in the saphenous or femoral vein percutaneously or by cutdown. The former may be accomplished by a sheath method such as that devised by Desilets and Hoffman (25). A 6 F sheath serves for a 5 F catheter and a 8 F sheath for a 7 F catheter.

In view of these previous successful experiences, duplicated in this difficult case after several previous failures, I recommend this catheter in the diagnostic study of TGA and similar complex heart cases. Catheterization of patients with cardiac arrythmias, such as Ebstein's anomaly with the Wolff-Parkinson-White syndrome, might be less hazardous than with the standard catheters *.

** The patient has subsequently undergone cardiac surgery, consisting of a Mustard procedure and repair of the VSD (32).*

Summary

The successful application of a Swan-Ganz balloon-tipped, flow-directed catheter to attain pulmonary artery entry in an adult patient with transposition of the great arteries, ventricular septal defect and pulmonary stenosis is reported. A review of the pertinent literature is made.

Resumen

El uso exitoso del cáteter de Swan-Ganz para obtener la entrada a la arteria pulmonar en un paciente adulto con transposición de los grandes vasos, defecto interventricular y estenosis pulmonar se presenta en este informe. Un repaso de la literatura pertinente se incluye.

Acknowledgment

To Dr. Luis M. Rodríguez Mora for his help and his vital role in the cardiac catheterization.

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LUNG TRANSPLANTATION: AN ANALYSIS OF THE MORPHOLOGICAL, FUNCTIONAL AND BIOCHEMICAL RESPONSE FOLLOWING ISCHEMIA AND PRESERVATION

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Since the first clinical lung transplantation performed in 1963 by Hardy and his associates (24), significant advances have been made in experimental auto-and allografting of the lung. Veith and Koerner (70) have recently reviewed the present stand of our knowledge. They pointed out that there are two major obstacles to success besides technical problems. Firstly, the problem of rejection which has not been solved and secondly there are no reliable methods of lung preservation available. In this paper we review the effect of ischemia and preservation on the anatomic, functional and biochemical response of the transplanted lung.

From the ideal point of view, a successfully preserved organ should be able to assume its full physiologic and biochemical functions after transplantation and maintain its microscopic and ultramicroscopic structure. Minor and reversible morphological changes may be tolerable, as long as they do not interfere with the organ function. In case of the transplantation of an organ for which an extracorporeal support system is not available and whose immediate function is vital to the patient the requirements are even more stringent. Besides the heart, the lung has to function immediately after transplantation since the patients with end-stage lung disease will nearly exclusively depend on the graft.

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Morphological Pulmonary Response After Ischemia

In evaluating the adequacy of lung preservation morphological criteria are not helpful since microscopic and ultramicroscopic changes after shorter periods of ischemia are relatively few. After approximately 6 hours of hypothermic perfusion Milhaus and his colleagues (36) did not find any significant ultra-structural changes. After extended ischemia Hino and his associates noted bronchiolitis obliterans and thickening of blood vessel walls (26). Fonkalsrud and colleagues (17) also observed alveolar thickening, filling of the alveolar spaces, and interstitial and intraveolar hemorrhage after ischemia of over 6 hours. Payan and his associates (41), found severe ultrastructural changes in the basal membranes, endothelial cells and pneumocytes after 5 1/2 hours hyperbaric, hypothermic preservation. There was an edema of the septae with rupture of the basal membranes, collapse of the capillaries, numerous vesicular inclusions in the cytoplasm, and disappearance of the fine structure of the mitochondriae.

Functional Pulmonary Response After Ischemia

Most of the morphological changes are usually preceded by functional impairment. If a lung is subjected to an intolerable period of ischemia pulmonary edema occurs as soon as the blood supply is reestablished. If an experimental animal survives the initial period, a depression of pulmonary function can be observed (1, 49, 51, 69).

Fonkalsrud and his group (17), noted that the contribution of the left lung to ventilation dropped from 46 percent to 39 percent measured 3 days after 3 hours of normothermic ischemia. If the ischemia was exten-

ded to 4 hours the left lung contributed only 33 percent and after 5 hours of ischemia only 24 percent to the total pulmonary function. After a 3 week period the lung previously rendered to ischemia recovered and contributed again approximately 45 percent to the gas exchange. If the ischemia was extended over 5 hours the depression of pulmonary function was more severe (only 12 percent contribution of the left lung) and there was no recovery after 3 weeks (17). These observations are similar to the results obtained by Garzon and his group (19, 20), after 24 hours of hypothermic preservation the contribution of the previously ischemic left lung to the total pulmonary function decreased to 33 percent as indicated by minute volume and to 31 percent as indicated by oxygen consumption. After normothermic ischemia, however, the lung was only able to recover after an ischemia period up to 2 hours. If the hilar occlusion was extended over this period a permanent loss of function occurred (20). Most authors could not demonstrate a permanent loss of pulmonary function after the lung had been rendered ischemic under different conditions. Goldstein and his associates (21), found no permanent alteration in minute venitlation and oxygen consumption after hypothermic hyperbaric storage for 24 hours. Similar results were obtained by Arnar and his colleagues(2), in baboons whose lungs were subjected to 3 hours of ischemia at room temperature and then reimplanted. After temporary depression of all parameters the ventilatory function returned to normal after several weeks. Only Hino and his group (26), observed a permanent depression of tidal volume, minute volume, and oxygen uptake after hypothermic (0-4° C), hyperbaric (3 atm) ischemia of the lung for 24 to 96 hours. Such massive suppression in pulmonary function, even if only temporary would not be tolerated in a clinical situation in which the graft carries nearly the entire respiratory load. The observations about hemodynamic alterations are more equivalent. Goldstein and his associates (21), did not find any change in main pulmonary artery pressure and Arnar (2) showed only an insignificant increase after pulmonary ischemia. Hino (26), on the other hand, demonstrated a higher pulmonary vascular resistance after the lung was subjected to ischemia and reimplanted and a significant rise in left pulmonary artery pressure on occlusion of the right pulmonary artery. Fonkalsrud and his group (17), also observed a rise in pulmonary artery pressure after the lung was subjected to 6 hours of normothermic ischemia. Veith and his associates (66), stated that functionally adequate transplants have normal pulmonary vascular resistance. If the blood flow to the transplanted lung is increased by vasoconstriction of the opposite lung the pulmonary vascular resistance drops in an adequately transplanted lung but rises in inadequate transplants (66). In judging the specificity of these alterations of pulmonary morphology and function one should keep in mind that similar changes are described as reimplantation response in autografted lungs not subjected to extended ischemia (4, 30, 45, 46, 52, 55, 65). It is difficult to determine if the above described depression in pulmonary function and the elevation of the pulmonary vascular resistance are due to ischemia, denervation, or other insults to the lung, or a combination of several factors.

Biochemical Pulmonary Response Following Ischemia

The most striking biochemical change in an ischemic lung is an immediate drop in glucose content and consumption. Wichert (71) showed that the glucose content of the rabbit lung dropped from 3.13 umol in the normal state to 0.067 umol after 180 minutes of warm ischemia. The pyruvate content dropped under the same conditions from 0.299 μmol to 0.128 μmol. The lactate rose from 1.13 μmol to 12.05 μmol which caused a rise in the lactate/pyruvate quotient from 4.9 to 94.1. Parallel to these changes in glucose and its metabolites, the adenosine triphosphate (ATP) content dropped from 1.53 μmol to 0.25 μmol and the adenosine monophosphate (AMP) concentration rose from 0.15 μmol to 0.49 μmol with the adenosine diphosphate (ADP) being relatively constant at 0.44 μmol and 0.32 μmol respectively. The total content of phosphonucleotides decreased from 2.12 μmol to 1.05 μmol (71). Shimada and his associates (44), noted that the glucose consumption decreased from 9.41 umol/g/hr. to 4.77 umol/g/hr. after 6 hours of ischemia. Parallel to this the oxygenation rate as measured by the production of ^{14}C labeled CO_2 dropped from 2.21 umol/g/hr. to 1.10 umol/g/hr. for glucose and from 23.25 umol/g/hr. to 2.55 umol/g/hr. for acetate after 24 hours of ischemia (44). Both observations show that the lung is very sensitive to ischemia due to the fact that it only uses glucose for its energy exchange and that its content of carbohydrates is rather limited. On the other hand, the content of phospholipids does not change remarkably during is-

chemia (24.30 μmol before and 27.25 μmol after 180 minutes ischemia). There is also no change in the content of the different fractions of phospholipids as: sphingomyelin, phosphatidylcholin, phosphatidylserin, phosphatidylinositol, and phosphatidylanolanine (71). This observation is important since the phospholipids are part of the surfactant system, but due to the ample supply of these substances it can be expected that the surfactant system withstands prolonged periods of ischemia. From the biochemical standpoint the tolerance of the lung to ischemia is limited to 2 hours since at this time the lungs' supply of glucose and ATP is exhausted.

Length of Tolerance of the Lung to Normothermic Ischemia

The lung's functional tolerance to normothermic ischemia is rather limited. Blades and his group (6), noted that the pulmonary function deteriorated rapidly and after 30 minutes of ischemia the lung was not able to adequately function. Hankinson and Edwards (23), found a tolerance to normothermic ischemia of 1 hour and Borrie and Lichter (9), reported 2 hours of ischemic tolerance. In general, one can assume that the collapsed lung tolerates 30 minutes of ischemia at body temperature without impairment of function. As shown by Veith and associates (68), this period can be extended to 3 hours when the lung is ventilated, and to 4 hours when the lung is inflated. In Veith's experiments the contralateral pulmonary artery was ligated immediately after the period of ischemia to make the animal completely dependent on the lung previously rendered ischemic (68). Similar experiments were done earlier by Stevens and his associates (48) who noted that the survival of dogs after the transplantation of a lung which was rendered ischemic for 24 hours could be extended over 24 hours when the lung was ventilated during ischemia. In these experiments the contralateral pulmonary artery was not ligated (48). These observations have been confirmed in primates by Joseph and his collaborators (29). Baboons tolerated normothermic ischemia of the inflated lung for 4 hours and of the ventilated lung for 5 hours with immediate contralateral pulmonary artery ligation (29). It is generally agreed upon in the literature that ventilation enhances the tolerance of the lung to ischemia regardless which method of preservation is used. Only Ross and Alves (42) obtained different results. He subjected a dog lung to 2 1/2 hours of hypothermic ischemia combined with hyperbaria and obtained better preservation as tested by animal survival with the lung ventilated or inflated (42). There are only speculations about the reason for the beneficial effect of ventilation and inflation. Stevens and his associates (50), found that prevention of lung collapse below the functional residual capacity is sufficient to prolong tolerance to ischemia. They speculated that the surfactant system is damaged as soon as the lung collapses completely, resulting in a severe depression of pulmonary function after reestablishment of the blood flow (50). Lately, Fonkalsrud and his group (18), were able to increase the survival time of dogs who underwent hilar occlusion by the use of + 5 cm H_20 PEEP to a mean of 51.4 days compared with a survival time of 9.3 days with inflation. They claimed an increase of the tolerance of the lung to normothermic ischemia to 10 hours by ventilation with PEEP (18). Lungs which were left in situ after the death of the donor could be preserved for longer periods of time. In vitro studies showed that a lung ventilated with room air for 6 hours in a cadaver was able to provide an efficient gas exchange as measured by oxygenation of desoxygenated blood (27). Veith and his group (65), showed that a lung that remains in a donor dog after death for 18 hours can provide adequate pulmonary function if mechanical ventricular assistance is used in the donor.

Methods of Organ Preservation

After we have reviewed the morphological, physiological, and biochemical changes resulting from lung ischemia we are able to define the criteria of a successful lung preservation more precisely: 1) The morphological integrity, especially of the capillary-alveolar barrier has to be maintained, 2) the depression of the pulmonary function, even for a short period must be avoided; and 3) the metabolism has either to be inhibited to prevent the build-up of metabolic end products and break-down of energy stores or metabolic substrate for aerobic metabolism must be supplied and end products removed.

There are basically 2 methods of organ preservation: metabolic inhibition and metabolic maintenance. The first can be achieved by hypothermia and pharmacological agents, the latter by perfusion in vitro or in vivo or by hyperbaria. Both methods have been shown to be of value in the preservation of kidneys and other organs.

Kidneys could be preserved by perfusion cooling for 30 hours and functioned immediately (13, 43). It has also been shown that metabolic inhibition with allopurinol is possible in several organs (57). The most successful method for organ preservation seems to be pulsatile perfusion which allows a safe preservation period up to 48 hours (56, 58, 59). When one applies these principles to lung preservation one should keep in mind that an immediate and full function of the preserved lung is mandatory. Methods for extracorporeal support for respiratory insufficiency are available and promising, but the use of the membrane oxygenator cannot be regarded as safe and as routine as for example hemodialysis (25, 72).

Lung Preservation by Metabolic Inhibition

Metabolic inhibition in preservation of the lung has nearly exclusively been achieved by hypothermia. Freezing of the lung at subzero temperatures or by fluorocarbon resulted in massive morphological and functional damage incompatible with life (35, 39). Magnesium ions were the only means ever used in pharmacological metabolic inhibition of the lung, but the results were not convincing (53).

A prolonged time of ischemic tolerance by hypothermic storage was first achieved by Conaughton and his associates (14) and Blumenstock and his group (7, 8). Conaughton and his associates subjected dog lungs to ischemia at different temperatures and showed the tolerable ischemia time at 10° C being 6 hours. Since all dogs tolerated a subsequent contralateral pneumonectomy, the pulmonary function was assumed to be sufficient (14). Blumenstock and his group (7), preserved lungs for 18 to 28 hours of 4° C replacing the pulmonary blood with plasma and ventilating the bronchus with room air. The histological structure was preserved in 4 of 6 cases (7). Similar results were obtained by Joseph and his colleagues (29) in baboons which tolerated autotransplantation with immediate ligation of the contralateral pulmonary artery after preservation of the inflated lung for 5 hours at 10° C. Extension of cold ischemia to 20 hours does not result in any changes in morphology or surface tension, but reimplantation does yield less satisfactory results, only 7 out of 25 animals survived 7 days (54). In situ hypothermia obtained by perfusion with Ringer's lactate was tolerated for 2 hours as tested by bilateral allotransplantation. Perfusion with cryoprecipitated plasma at the same temperature did not extend the tolerable ischemia time, whereas perfusion with Sack's solution yielded a preservation time of 5 hours (31). The most consistent results in pulmonary preservation by hypothermia are reported from the laboratory of Noirclerc (16, 22). Forty-three out of 48 dogs who received allotransplants after a 24 hour preservation showed immediate adequate function of the transplanted lungs. It should be noted, however, that the dogs were not subjected to immediate contralateral pulmonary artery ligation. The authors attribute their success to the following details in technique: 1) heparinization of the donor; 2) flushing of the pulmonary vasculature with 250 to 500 cc Collins III solution at a pressure of 40 cmH_2O; 3) ventilation of the lung during flushing to prevent atelectasis; 4) preservation of 4° C completely submerged in Collins III solution; 5) fast implantation to minimize warm ischemia, and 6) avoidance of pO_2 above 150 mmHg at any time since higher partial oxygen pressures induce pulmonary edema in the experience of the authors (16, 22). Crane and his associates (15), have recently reported successful transplantation of lungs stored up to 24 hours in Collins-Sacks solution with immediate ligation of the pulmonary artery on the contralateral side.

Pulmonary Preservation by Metabolic Maintenance

Hyperbaria has been added to hypothermia by several authors, but has not generally been able to prolong the safe preservation period significantly. Blumenstock and his group (8), flushed lungs with low molecular weight dextran and placed them in a hyperbaric chamber with 100 % O_2 at a pressure of 30 lbs/sq inch at 4° C for 24 hours. The lungs were then allografted to 32 recipient dogs. Twelve dogs died immediately postoperatively presumably of technical failures, 2 dogs died later of unexplained causes, and 8 dogs survived 6 to 72 days. Largiader and his group (32, 33, 34), preserved lungs under similar conditions for 24 hours and reimplanted them with good results in 8 dogs. They conserved the lungs at 4° C and 3 atm oxygen and used a salt glucose solution containing 5 percent low molecular weight dextran, 100 mg/L heparin, and 0.03 percent tromethamine

adjusted to a pH of 7.4 with $NaHCO_3$. They pointed out that oxygen pressure above 3.8 atm results in lung damage due to oxygen toxicity (32, 33, 34). Similar results have been obtained since then by several authors, and pulmonary function tests in survivors showed no permanent alteration (38, 42). However, Brownlee and Couves (10), were not able to demonstrate any beneficial effect of hyperbaria added to hypothermia and Jirisch and his associates (28), found left lower lobes preserved for 24 hours at 4° C and 2 atm O_2 functionally insufficient when tested as a source of oxygenation in an extracorporeal circulation system.

Nonpulsatile perfusion in vitro has been disappointing since it resulted invariably in pulmonary edema inconsistent with life. In early experiments Veith and his group (63, 64), showed that an isolated lung could be perfused with homologous blood for 6 hours with preservation of the pulmonary architecture, but longer perfusion resulted in histologic alterations. Vanderhoeft and his associates (61, 62), found that hypothermic perfusion was superior to surface cooling in achieving a homogenous hypothermia of the lung, but perfusion with a solution containing 2 vol percent O_2 was unsuccessful. Most authors noted a weight gain and pulmonary edema inconsistent with the life of the experimental animal, but after a short period changes could not be shown on electron microscopy. The edema occurs usually after 3 to 4 hours regardless if the lung is perfused with electrolyte solution, low molecular weight dextran, or plasma (11, 12, 36, 47). There are only a few reports which claim a beneficial effect of perfusion. Otto and his associates (40), obtained slightly better results with perfusion with blood diluted with low molecular weight dextran for 2 to 24 hours than with deep hypothermia. The perfusion was tolerated for approximately 5 hours (40). Modry and his group (37), perfused 13 ventilated left lower lobes with glucose enriched blood at 28° C and could demonstrate good gas exchange after 16 hours. Transplantation of 3 lungs subjected to extended hypothermic perfusion with heparinized blood at 28° C for 14 hours was successful and the lungs showed normal pulmonary function (37).

All the previous observations were obtained with nonpulsatile perfusion systems. Recently Toledo-Pereyra and collaborators (60), subjected lungs to hypothermic pulsatile perfusion with different perfusates, perfusion pressures, and different forms of ventilation or inflation. The outcome of the perfusion was tested in vitro by systolic perfusion pressure, flow, vascular resistance, weight gain, and determination of LDH, lactic acid, SGOT, oxygen, and glucose consumption as well as pulmonary water content and histology. The best results wree obtained when the lungs were perfused with a modified silica gel fraction (SGF) of plasma which consisted of 900 cc SGF, 200 cc salt poor albumin, high concentrations of glucose and potassium at a systolic perfusion pressure of 2.5 mmHg and inflation with 100 percent N_2. After 72 hours of perfusion flow and systolic perfusion pressure were minimally changed, and vascular resistance showed only a slight increase after 24 hours. There was a moderate decrease in oxygen consumption, glucose consumption and pH, and a moderate increase in weight, LDH, SGOT, and lactic acid. Histologic studies showed a well preserved alveolar architecture without alveolar-capillary disruption or intraalveolar hemorrhage. The edema formation was minimal. This in vitro model awaits testing in vivo but the new aspects of this study included: (a) low perfusion pressure, b) intracellular perfusate nearly totally free of lipoproteins and fibrinogen, (c) high protein content, and (d) high perfusate osmolarity. All these changes concurrently contributed to a better function of the perfused lung.

In short, it is evident that much work still remains in improving the methods for normothermic or cold ischemic protection and the techniques for successful lung preservation.

Summary

Some of the obstacles for successful lung transplantation include the lacking of acceptable methods for ischemic protection and the absence of reliable systems for preservation. The lung response to 60 minutes of warm ischemia basically consists of alveolocapillary edema and disrupture, mitochondria swelling, interstitial hemorrhage, significantly depressed pulmonary function, elevation of pulmonary vascular resistance and considerable drop in glucose, phospholipids and adenosine triphosphate (ATP). The tolerance to warm ischemia has increased to several hours with the use of different ventilatory assistance with or without positive and expiratory pressure. Several methods of preservation have been attempted: hypothermia, hyperbaria and hypothermic pulsatile or nonpulsatile perfusion. Hypothermic pulsatile perfusion appears to offer longer

periods of protection than the other methods. New advances on the use of drug protection during warm ischemia and the utilization of intracellular colloid or noncolloid solution for hypothermic storage, probably will extend the limits of ischemia and preservation to longer periods of time.

Resumen

La falta de métodos adecuados de protección pulmonar durante la isquemia y la ausencia de buenos métodos de preservación son algunos de los múltiples problemas que no se han resuelto para el transplante pulmonar. Después de 60 minutos de isquemia caliente el pulmón responde con edema de las mitocondrias, hemorragia intersticial, edema alveolo-capilar, resistencia vascular elevada, disminución de la reserva pulmonar, y baja en los niveles de glucosa, fosfolípidos y trifosfato de adenosina (ATP). El uso de diferentes sistemas de asistencia ventilatoria con o sin presión final expiratoria positiva han permitido una mayor tolerancia a la isquemia caliente. Varios de los métodos de preservación utilizados son: hipotermia, hiperbaria e hipotermia con perfusión pulsátil o no pulsátil. La hipotermia con perfusión pulsátil aparece ofrecer los mejores resultados. Sin embargo, el uso de drogas para proteger el pumón durante la isquemia caliente y la utilización de soluciones de coloide intracelular probablemente mejorarán los límites de isquemia y preservación.

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SHORT TERM PROGNOSTIC IMPORTANCE OF HEMODYNAMIC PARAMETERS IN ACUTE MYOCARDIAL INFARCTION

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Acute myocardial infarction (AMI) may lead to a fatal outcome by one of three mechanisms; arrythmias, pump failure or rupture of the heart. The development of the coronary care unit (CCU) has permitted prevention, detection and treatment of the electrical instability of the acutely infarcted myocardium. It is now also possible to measure intracardiac pressures in the acutely ill CCU patient (1). These measurements may give us an indication of the degree of left ventricular dysfunction present in these patients. A major determinant of the degree of left ventricular dysfunction and mortality is the size of the myocardial infarction (2). Thus the degree of left ventricular dysfunction may allow indirect assessment of infarct size and mortality. This study correlates short term prognosis with parameters which may be obtained by physical examination, chest x-rays and right heart catheterization.

Materials and Methods

Fourteen male patients underwent bedside right heart catheterization in the acute phase of myocardial infarction. The diagnosis was established by a history of chest pain, rise in serum enzymes (serum glutamic oxaloacetic transaminase, creatine phosphokinase and lactic dehydrogenase), diagnostic electrocardiographic changes or history of chest pain with enzyme elevation in the presence of an old or new conduction disturbance. Right heart pressures were monitored via a Statham P-23-1-A transducer to an American Optical amplifier with oscilloscope and pressure gauge. Pressures and cardiogram were recorded with a Sanborn two channel recorder. Systemic blood pressure was determined by the cuff method. The presence of abnormal auscultatory findings was documented by one of the authors. Chest x-rays were obtained in all the patients. In the majority of the patients the x-ray was taken within 24 hours of the catheterization. The x-rays were read by one of the members of the radiology department who was not familiar with the clinical data. Special emphasis was placed on the presence of cardiomegaly, or pulmonary congestion.

Short term survivors were defined as those who left the hospital alive or who survived in the hospital a minimum of 30 days. Pulmonary capillary wedge pressure (PCW) was obtained in all but three cases- in these cases pulmonary artery diastolic pressure was used as an index of pulmonary capillary wedge pressure.

Results

Fifteen separate episodes of acute myocardial infarction were documented in fourteen patients. Fifteen separate hemodynamic studies were carried out. Twelve patients survived 30 days or left the hospital alive. Three patients died within 48 hours of admission to the coronary care unit. The mean age of the fifteen patients was 58. (range 43-86.)

For all fifteen patients hemodynamic parameters were better determinants of survival than the individual presence of S3 filling sound, pulmonary rales, the presence of cardiomegaly or pulmonary congestion as determined radiologically.

Figure 1 shows that S3 or rales were present in all the patients who died and also in 83 percent of the patients who survived the infarct. Also shown in this figure is the incidence of cardiomegaly, congestive heart failure or pulmonary congestion in survivors versus non survivors. Although the x-ray findings were found in all the fatal cases, abnormalities were also seen in 50 percent of the survivors.

Figure 2 shows that systolic blood pressure was significantly lower in two of the subjects who died as compared to the survivors. Extreme hypotension (systolic

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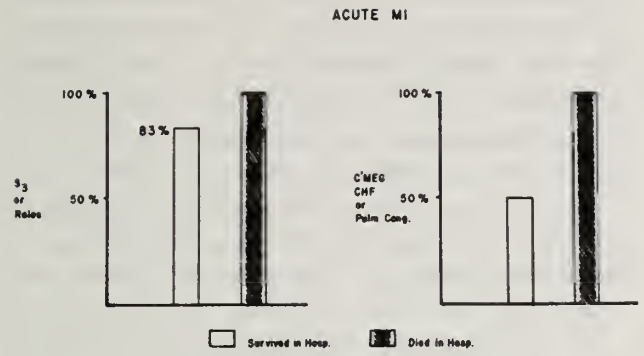


Figure 1: *Incidence of S3 filling sound, rales, radiologic evidence of cardiomegaly, congestive heart failure or pulmonary congestion in survivors and non survivors.*

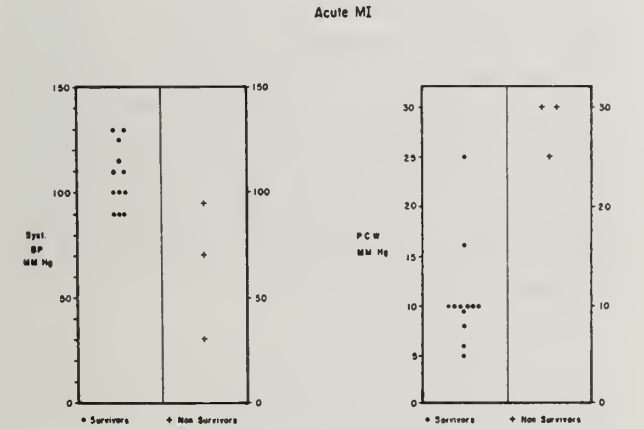


Figure 2: *Systolic blood pressure in survivors and non survivors. Although the systolic blood pressure in the non survivors was markedly lower than in survivors one of the subjects who expired cannot be distinguished from the survivor group. A similar observation was made when pulmonary capillary wedge (PCW) was utilized as an index of survival.*

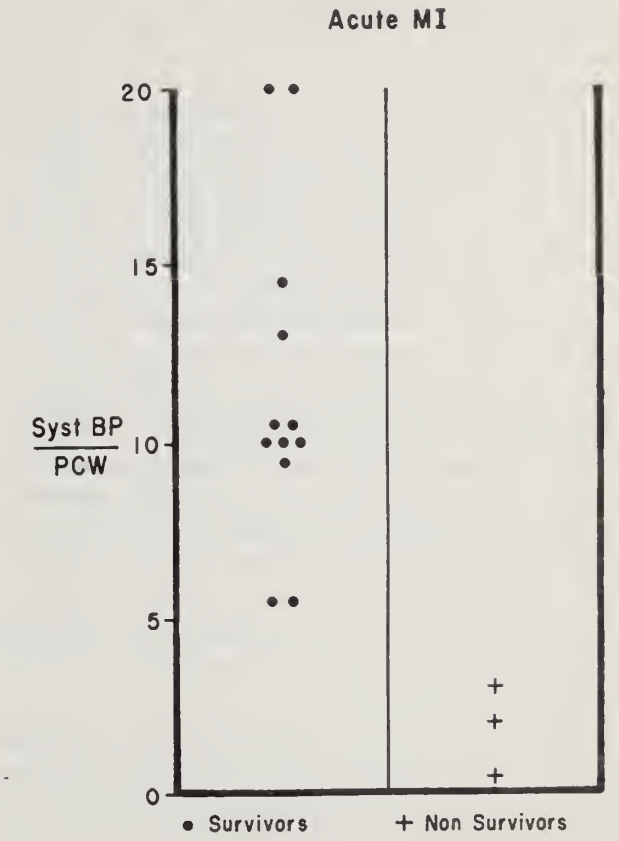


Figure 3: *Systolic blood pressure to pulmonary capillary wedge pressure ratio in survivors and non survivors. There is a clear distinction between the two groups.*

blood pressure less than 85mmHg.) was always associated with cardiogenic shock and death. Moderate hypotension (Syst. BP 85-100) was seen in both groups of patients. Six of the seven moderately hypotensive patients survived and one died. None of the patients with normal systolic blood pressure (Syst. BP > 100) died. Severe hypotension was always associated with a poor prognosis but moderate hypotension was not uniformly associated with death. Pulmonary capillary wedge (PCW) pressure was also a determinant of survival. None of the patients with a normal PCW (less than 12mmHg) died. An abnormal PCW was not always associated with a poor prognosis. A PCW of 25 mmHg was seen in one of the survivors as well as one of the non survivors. None of the patients with a PCW of over 30 mmHg survived.

Figure 3 shows that by combining these two hemodynamic parameters into a systolic BP/PCW pressure ratio we are able to better separate survivors from non survivors. All of the patients who survived had a BP/PCW ratio of five or more. None of the patients with BP to PCW ratio less than 5 survived the myocardial infarction.

Discussion

Swan, Ganz and Forrester introduced the concept of a balloon tipped floating catheter which would facilitate bedside right heart catheterization without fluoroscopic monitoring (1). Since then it has been proven that right atrial or central venous pressure in patients with acute myocardial infarction does not reflect pulmonary venous distending pressure (3). The central venous pressure (CVP) may be actually misleading in this condition where fluid and diuretic management are of critical importance. Pulmonary capillary wedge pressure has been used as an index for optimal left ventricular performance in acute myocardial infarction (4). The depression of left ventricular performance is proportional to the area of involved left ventricular mass in acute myocardial infarction (2, 5). The area of involved tissue is probably the major short term prognostic determinant in acute myocardial infarction (5).

Radiologic phenomena are influenced by a number of variables such as time lag between changes in hemodynamic pressures and subsequent accumulation or clearance of interstitial fluid (4). This may be the main cause for the poor prognostic ability of the x-ray in the acute episode of myocardial infarction. Auscultatory phenomena have a large subjective factor and a number of pulmonary processes may further confuse the picture.

The individual hemodynamic parameters studied are accurate determinants of short term survival. Severe hypotension is usually due to cardiogenic shock and carries a poor prognosis. Moderate hypotension does not always imply a severely depressed myocardium. It may be due to hypovolemia with low cardiac output secondary to decreased left ventricular preload. These patients will have a better prognosis, if adequately managed, than the patient with early cardiogenic shock and moderate hypotension.

When comparing left ventricular filling pressure with survival it is noted that patients with a normal PCW pressure have a much better short term prognosis than patients with a markedly elevated PCW pressure. Not all the patients with an elevated PCW pressure fell in the poor prognostic group. Pulmonary capillary wedge pressure may at times be a reflection of left ventricular afterload as well as an index of left ventricular performance (6). Thus an elevated PCW pressure may reflect a high left ventricular afterload due to elevated total peripheral resistance. These patients will demonstrate high PCW pressures, normal or high systolic pressures.

By combining both of these hemodynamic parameters a much better prognostic index was found between the systolic BP/PCW pressure ratio and survival. The left ventricle works as a pressure amplifier by converting the end diastolic or filling pressure into a systolic pressure by means of its mechanical action. The systolic BP/PCW ratio reflects the efficiency of this mechanical amplifier and therefore, is a sensitive index of the efficiency of the left ventricular pump.

In our patients with acute myocardial infarction who did not survive, the average systolic BP/PCW ratio was 2.2 indicating a very low pumping efficiency, i.e. - the left ventricle was only able to amplify or augment the filling pressure by a factor of 2.2 via the force of its mechanical contraction. This mechanical augmenting factor was approximately five times higher in the survivors. This is in accordance with the recently published work by Verdowu, Hagemeijer and Van Drop (7). These authors, using a larger group of patients correlated short term survival with an index derived from the ratio of diastolic blood pressure over PCW pressure times mixed venous oxygen saturation. Their results closely match the result of this study. Whether these hemodynamic parameters can be directly correlated to other indices of acute myocardial infarct size is yet to be investigated.

Summary

Fourteen patients with fifteen episodes of acute myocardial infarction underwent chest x-ray and hemodynamic studies. Physical and radiologic signs of heart failure were poor determinants of short term survival. Systolic blood pressure and pulmonary wedge pressure were better determinants of short term survival; however, the calculated systolic blood pressure to pulmonary capillary wedge pressure ratio was the best short term prognostic indicator. These hemodynamic parameters may be a reflection of infarct size.

Resumen

Catorce pacientes que habían sufrido un total de 15 episodios de infarto agudo al miocardio fueron exami-

nados por medios radiográficos y hemodinámicos. Los índices de examen físico como los índices radiológicos de fallo congestivo fueron determinantes pobres de la supervivencia a corto plazo de estos pacientes. La presión sistólica arterial y la presión pulmonar en cuña fueron mejores determinantes de la supervivencia a corto plazo. La razón entre la presión sistólica arterial sobre la presión pulmonar en cuña, fue la mejor índice pronóstico de supervivencia a corto plazo. Estos parametros hemodinámicos puede que sean reflejos del tamaño del infarto agudo.

Acknowledgment

We are indebted to Dr. Manuel Martínez Maldonado for his advice and review of the manuscript.

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UNILATERAL HYPERLUCENT LUNG (SWYER-JAMES SYNDROME)

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The unilateral hyperlucent lung is an unusual and interesting cardio-pulmonary disease that was described in 1953 by Swyer and James (1). The purpose of this report is to describe briefly the different aspects that characterize this disease. A case studied by the authors is presented as an example.

Case Report

A. M. V., a 56-year old nonsmoker housewife, was first evaluated by us in October 1975. She had been treated for "bronchial asthma" since she was three years old. There was a lifelong history of cough productive of abundant purulent sputum, wheezing, and frequent respiratory infections. Small hemoptysis had been present for the last three years. Dyspnea was present only on heavy exertion. On physical examination the patient was a robust, healthy looking female. The abnormal findings were limited to the chest. There was dullness, decreased tactile fremitus and breath sounds, and fine rales over the left hemithorax. The heart examination was normal. The extremities showed no clubbing, cyanosis, or edema.

The hemogram, urinalysis, blood chemistry studies (SMA-12), and the electrocardiogram were normal. The arterial blood gas measurements performed while the patient was breathing room air showed a pO_2 of 71 mmHg., a pCO_2 of 42 mmHg., and a pH of 7.43. Pulmonary function studies (Table I) showed severe airway obstruction. A chest roentgenogram (Figure 1) showed a radiolucent, avascular, small left lung and hypervascularity of the right lung. The heart and mediastinum were displaced to the left side. Bronchography (Figure 2) showed mild bronchiectatic changes with grouping and contraction of all the branches of the left lower lobe and the inferior segment of the lingula. There was no alveolar filling. At cardiac catheterization the left pulmonary artery was entered with ease thus ruling out its absence. Pressures (in mmHg.) were as follows: right atrium, mean 12; right ventricle, 44/13; main pulmonary artery, 37/16, mean 23. A dextroangiocardiogram (figure 3) showed marked attenuation of the left pulmonary artery and its branches and normal vascularity of the right lung. A perfusion lung scan with ^{131}I-macroaggregated albumin showed absent perfusion of the left lung.

Medical observation and treatment of intercurrent infections was recommended.

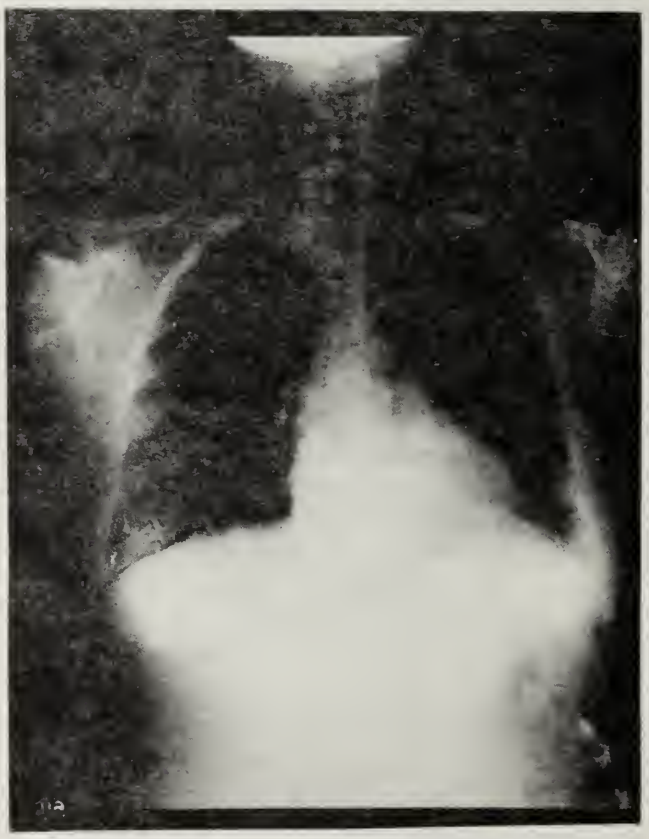


Figure 1: *Chest roentgenogram. There is hyperlucency of the left lung with decreased vascular markings. The mediastinum is displaced toward the left side.*

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TABLE I
RESULTS OF PULMONARY FUNCTION STUDIES

Measurement	Observed	Predicted
Total Lung Capacity (mL)	2506	3460
Vital Capacity (mL)	1541	2380
Functional Residual Capacity (mL)	1171	1960
Maximal Voluntary Ventilation (L/min.)	40	72
Forced Expiratory Volume in one second (L)	0.75	1.70
Maximal Mid Expiratory Flow Rate (L/sec.)	0.67	2.3
Diffusion Capacity to Carbon Monoxide (mL.min./mmHg)	9.4	11.9

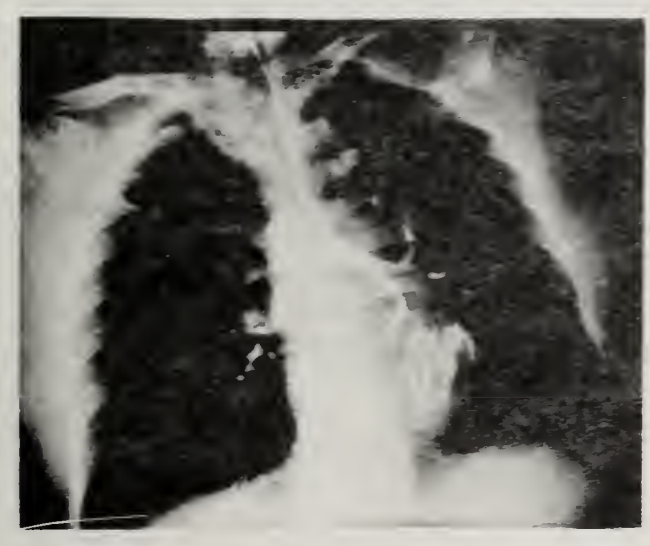


Figure 2: *Bronchogram. There is bronchiectasia and no alveolar filling on the left lung.*



Figure 3: *Dextroangiocardiogram. There is marked attenuation of the left pulmonary artery and its branches.*

Discussion

The unilateral hyperlucent lung derives its name entirely from the manifestations it produces roentgenografically. The characteristic radiographic signs are: (2) 1) chest roentgenography-There is unilateral hyperlucency on the affected lung with normal or decreased volume. diminished vascular markings. and a small hilar shadow. The mediastinum is displaced to the affected side on inspiration but on expiration swings back toward the normal side without any change in the volume or density of the affected lung, indicating the presence of air trapping in the diseased lung. Saleh et al (3) have shown that in the presence of left ventricular failure the congestive changes will occur only in the normal lung: 2) Bronchography-The major bronchi are normal. On the affected side there is bronchiectasia and clubbing of the most peripheral bronchi, with obstruction to filling by contrast medium of the terminal bronchioles and alveoli: 3) Pulmonary angiography-There is diminution in the pulmonary vascularity of the affected side: 4) Bronchial arteriography-Gottlieb and Turner (4) have recently demonstrated

by selective bronchial arteriography and scintinography that the bronchial circulation to the affected lung is increased; 5) Lung scintinography-As expected, there is absent perfusion on the affected side and delayed washout of the ^{133}Xenon in the ventilation scan.

The disease may present in different manners (5-8). The disease affects both sexes. It may occur in the right or in the left lung. The patients may be asymptomatic. More commonly, they develop frequent respiratory tract infections and have chronic cough productive of variable amounts of mucoid or purulent sputum. Some of them complain of hemoptysis and different degrees of physical disability. Others may have chest pain of a dull or pleuritic character, even in the absence of apparent pulmonary infection or pleural disease. The physical examination usually reveals decreased expansion of the thoracic cage on the affected side, dullness or hyperresonance to percussion, and decreased vocal fremitus and breath sounds. In addition, there may be rales and localized wheezing.

Pulmonary function studies (9-11) demonstrate the obstructive airway changes with reduction of the vital capacity and of the expiratory flow. The diffusing capacity may be normal or decreased, depending on the extension of the destructive pulmonary parenchymal changes. There is decreased elastic recoil of the lungs. The arterial blood gases may be normal at rest but usually are decreased during exertion. The decreased pulmonary arterial circulation causes an increase in the alveolar to arterial CO_2 gradient. Differential bronchospirometric studies show decreased ventilation and oxygen uptake in the affected lung.

The etiology of this entity has not been clearly defined. Currently, the predominant opinion is that the disease results from an inflammatory process that affects the smaller bronchi and bronchioles. The inflammatory process is usually of infectious origin (12, 13). However, two cases of unilateral hyperlucent lung have been reported after irradiation of the lung (14). The acute bronchiolitis leads to fibrosis and obliteration of the small airways. Chronic infection, bronchiectasia, and emphysema of the peripheral pulmonary parenchyma follows. The diseased lung then affects the pulmonary circulation. Interestingly, pathologic studies have demonstrated that the pulmonary vasculature is not as severely affected as it appears to be by angiography (1, 8). Another view upholds that a primary unilateral pulmonary vascular abnormality exists that predisposes to bronchial and alveolar changes (10).

After adequate radiological evaluation of the patient the physician will rarely have problems in the differential diagnosis of the unilateral hyperlucent lung. In obstruction of a pulmonary artery by an embolus or tumor the same plain x-ray appearance may be produced. The differentiation can be made on the basis of the clinical picture and normal bronchographic examination. Unilateral absence of a pulmonary artery can produce the same symptoms of the Swyer-James Syndrome and there will be a decreased volume of the affected side. However, the differentiation can be readily made by a normal bronchographic examination and the failure of a catheter to enter the affected pulmonary artery. The hilar shadow will be absent as compared to the small hilum present in the Swyer-James Syndrome. In compensatory emphysema of the hypogenetic lung syndrome the lung volume and hilar shadow will be increased in the hyperlucent side. The same holds true in unilateral obstructive emphysema, such as seen in aspiration of a foreign object. In this case bronchography will be invaluable in establishing the cause of the hyperlucency (2, 4).

In the majority of the patients with the unilateral hyperlucent lung the clinical course will be benign (5-8). Acute infections associated with bronchiectasia are managed in the usual manner. Lung resection should be reserved for those patients with serious infection, severe bronchiectasia, or pulmonary hemorrhage.

Summary

The characteristics of the Swyer-James syndrome were described. These include hyperlucency, bronchiectasis with absent alveolar opacification, and hypovascularity of the diseased lung. The clinical presentation, the pathogenesis, and the management were discussed. A case studied by the authors was presented as an example.

Resumen

En este trabajo se han descrito las características del síndrome de Swyer-James. Esta enfermedad se caracteriza por hipertransparencia, bronquiectasia con ausencia de llenado alveolar, e hipovascularidad del pulmón enfermo. Se ha discutido el cuadro clínico,

la patogenia y el tratamiento de la enfermedad. Un caso estudiado por los autores ha sido descrito con el propósito de ilustrar esta enfermedad.

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ANOFTALMIA Y DEFECTOS ESQUELETICOS: UN SINDROME DEFINITIVO

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Durante el último año, hemos estudiado 6 casos de anoftalmia y defectos esqueléticos de las extremidades, lo cual establece esta condición como un síndrome definitivo. Sus características son: faz peculiar, frente prominente, anoftalmia bilateral, blefarofimosis, septo y puente nasal prominentes, filtro alargado y micrognancia. Las manos muestran acortamiento bilateral del dedo 5 con hipoplasia de las eminencias tenar e hipotenar. Solo se encuentran 4 ortejos en cada pie. Radiológicamente se observan fosas orbitales llanas, fusión bilateral del 4 y 5 metacarpo, y ausencia bilateral de un metarso con su falange. También se observan anormalidades de severidad variable en la articulación radio-ulna proximal, lo cual limita la supinación. El desarrollo post-natal procede normalmente, salov por dificultad en aprender a caminar y a hablar. La presencia de retraso mental es difícil de cvaluar en estos casos, dada la severidad de las limitaciones físicas existentes. Las características familiares de la condición sugieren un patrón de herencia autosómico recesivo. Hasta donde tenemos conocimiento, esta condición ha sido descrita solamente una vez anteriormente por Masket, Galioto y Best, quienes en 1970 describen un niño de 2 9/12 años, hijo de una mujer puertorriqueña, con los signos característicos del síndrome.

CHRONIC LYMPHOPROLIFERATIVE DISEASE IN A YOUNG WOMAN WITH MARKEDLY FLUCTUATING LEUKOCYTE COUNT (WBC) AND PROMPT SUSTAINED RESPONSE TO CHLORAMBUCIL (CLB)

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A 29-year old female prescnted with a 15 month history of cervical lymphadenopathies. Multiple generalized lymphadenopathies were present. The WBC was 180,500 with 84 percent lymphocytes, mostly mature. The bone marrow was hypercellular with a lymphocytosis of over 95 percent. Cervical and axillary node biopsies revealed a well differentiated lymphocytic lymphoma (the histological equivalent of chronic lymphatic leukemia (CLL). Electron microscopy of pheripheral blood WBC was also compatible with CLL.

Because of a history of 4 relatives dying of tuberculosis, the patient was empirically given anti-tuberculous therapy. During this 6 month period, there was a marked fluctuation in the WBC, once dropping as low as 12,850 with 69 percent lymphocytes. There was an inverse relationship between the size of her lymph nodes and the WBC.

As no benefit was evident from anti-tuberculous therapy, this was discontinued. Two months later the WBC was 306,000 with 97 percent lymphocytes. Since the lymph nodes were also enlarging, the patient now had clearly progressive disease. Therefore, she was started on CLB 6mg and allopurinol 300 mg daily. Two weeks later, the WBC was 11,700 with 53 percent lymphs and the nodes were shrinking in size. After 2 more weeks of CLB, the WBC was 2,900 with 43 percent lymphs and there was no lymphadenopathy. After 10 months of treatment with CLB given every other month the patient remains in complete remission.

This case is of interest because 1) CLL is extremely rare in this age group; 2) a marked fluctuation in WBC has never been reported previously; 3) the inverse relation between the size of the lymph nodes and the

leukocyte count, which was apparently due to a compartmental shift in lymphocytes between the lymph nodes and the blood; 4) the dramatic response to alkylating agent therapy.

CONTRIBUCION DE LA MEDICINA NUCLEAR AL DIAGNOSTICO DE LA ENFERMEDAD POLIQUISTICA DEL HIGADO.

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Se sugiere la utilización de pruebas con materiales radioactivos: gamagrama, radioangiograma y gamagrama de la distribución sanguínea del hígado, como pruebas atraumáticas para aclarar el cuadro de poliquistosis en un paciente con hepatomegalia y pruebas funcionales negativas.

Se aconseja completar el estudio con ultrasonido para observar la consistencia de las lesiones y con gamagrama de riñón y pielograma endovenoso por la frecuencia en la asociación de la lesión hepática con poliquistosis renal.

Se presenta el ejemplo de un paciente estudiado en las condiciones descritas.

Luego de una breve discusión se concluye la posibilidad de confirmar el diagnóstico con las pruebas mencionadas sin necesidad de recurrir a otros medios más cruentos de exploración.

DNA ANTIGEN BINDING AVIDITY AND NEPHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS.

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Previous studies from this laboratory have shown a correlation between very high titers of anti-native deoxyribonucleic acid (nDNA) antibodies (AB) and active, severe nephritis in patients with systemic lupus erythematosus (Bol Asoc Med PR 67: 323-324, 1975). Some patients with high N-DNA binding did not manifest severe nephritis during their course and therefore studies of nDNA antigen binding curves by SLE sera were analized to compare nDNA binding avidity differences whcih could explain this observation. Six (6) SLE patients with high n-DNA binding (10 micrograms/ml) and severe nephritis were compared to six (6) SLE patients with high n-DNA binding but minimal (2) or no nephritis (4). Three (3) normal sera (2.5 micrograms/ml) were used as controls. N-DNA antigen binding avidity as measured by slope determination was significantly higher in patients with severe nephritis (mean = 755.2 mcgm/ml) than in those with mild or no nephritis (mean = 101.9 mcgm/ml) or in normal sera (mean = 6.6 mcgm/ml). These findings suggest an enhanced DNA-antiDNA immune complex formation due to increased antigen binding avidity as a possible explanation for observed differences in the incidence and severity of nephritis in SLE patients.

EXTREME DWARFISM SECONDARY TO SECKEL SYNDROME

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Seckel in 1960 informed of two patients with severe microcephaly and "bird headed dwarfism" as defined by Virchow's on the last century. Characteristics features of the syndrome are low birth weight, small head, prominent eyes, beaked nose, narrow face, marked dwarfism, mental retardation, multiple malformations and autosomal recessive inheritance. 27 cases have been informed in the literature.

Recently we had the opportunity to evaluate and perform endocrinologic work up to a two year female Dominican child, borne from consanguineous parents, with a birth weight of 3/4 pounds. Upon our evaluat. (2 years of chronological age) she presents a weight o 4 pounds and a height of 19 inches (the measurements of a premature baby), mild mental retardation, with slight to moderate motor retardation. Endocrine and other laboratory data exclusive of this child will be presented at the meeting.

ENFERMEDADES DE LA GLANDULA ADRENAL EN DOS NIÑOS PUERTORRIQUEÑOS

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Las enfermedades de la glándula adrenal en la población de niños puertorriqueños han sido evaluadas en los últimos seis años en el Centro Médico de Río Piedras. Nuestras estadísticas demuestran que la hiperplasia congénita adrenal es la entidad más frecuentemente encontrada en la infancia y la niñez. La pubarquia precoz fue excluída de estas estadísticas. En este estudio se evaluaron otras entidades adrenales raras como los tumores virilizantes y feminizantes, síndrome de Cushing, enfermedad de Adisson, deficiencia aislada de glucocorticoides, leukdistrofia adrenal, síndrome de Bartter y otras. Se enfatizará en los métodos de diagnóstico adecuados utilizados para detectar estas condiciones.

EXPERIENCE WITH A NEW SYNTHETIC ARTERIAL GRAFT

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Existing materials used as arterial substitutes do not satisfy all criteria of coagulation, patency, smoothness, tissue reaction and ease of use. We have evaluated a new vascular prosthetic material (expanded PolyTetraFluoro-Ethylene, P. T. F. E.) for replacmenet or bypass of large caliber, high-flow arteries in dogs.

A total of 21 mongrel dogs were anesthesized and subject to laparotomy. Either aortoiliac or aorto-aortic bypass were done using three different materials: Dacron, Microknit and PTFE. Evaluation criteria included: patency (pulses, aortogram, direct examinations); gross pathology; microscopic exam; technical ease.

Patency was the same in the three groups. P.T.F.E. was the most maneuverable, the most pliable, and the easiest one to suture. P. T. F. E., also caused minimal tissue reaction both grossly and microscopically when compared to Dacron. Also, P. T. F. E. did not require pre-clotting during surgery.

P. T. F. E. is an excellent arterial substitute which accomplishes at least the same patency rate of other synthetic arterial grafts with the advantages of better handling, minimal tissue reaction, no preclotting and ease of suturing.

FURTHER STUDIES IN MICE REGARDING A POSSIBLE VACCINE AGAINST BILHARZIASIS (Schistosoma mansoni)

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Preliminary studies in our laboratory have demonstrated that antigens of *Fasciola hepatica* adult worms which cross-react with *Schistosoma mansoni* protect CF-1 albino mice and golden hamsters against a challenge exposure with schistosome cercariae (Hillyer et al., *Bol. Asoc. Med. P. R.*, 67: 381-385, 1975; Hillyer, et al., *Fed. Proc.*, 35: 3013 A 1976; Hillyer, *Fed. Proc.* 35: in press 1976). The present investigations were designed to determine with these cross-reacting antigens the best immunizing schedule, route of inoculation and the effect of non-specific adjuvants such as Poly AU on protective immunity against *S. mansoni* using inbred CBA/J mice. A typical experimental protocol consisted of *immunizing* mice three times weekly with *F. hepatica* antigen and/or poly AU emulsified in Freund's Incomplete Adjuvant for 1-4 weeks, rested one week and then challenged with *S. mansoni* cercariae. Controls were administered Freund's adjuvant alone. The mice were bled 6 weeks later for the collection of serum and autopsied for the determination of worm burdens.

All of the mice in experimental groups immunized with *F. hepatica* adult worm antigen were protected against a challenge infection with *S. mansoni* cercariae when compared to unimmunized controls. The highest percent of reduction in worm burden was achieved in mice immunized three times a week for three weeks with *F. hepatica* whole worm antigen containing a total of 4.5 mg (dry weight) crude antigen where a 62 percent reduction in worm burdens was obtained. A non-specific adjuvant such as Poly AU achieved a 52 percent reduction while adding *F. hepatica* whole worm antigen to the inoculations increased the protection to 67 and

72 percent depending on the number of inoculations with Poly AU. A two to five-fold increase in antibodies against *S. mansoni* was observed in all immunized mice when compared to the unimmunized infected control at 6 weeks of infection. It is hoped that purification of these *F. hepatica* adult worm antigens that cross-react with *S. mansoni* will result in a more effective vaccine that can eventually be tested in higher vertebrates and protect against schistosome infections in man. These studies were supported by NIH Grant No. RR-8102 administered by the Division of Research Resources.

FREE AMINO ACID AND DIPEPTIDE ABSORPTION IN TROPICAL SPRUE

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Utilizing a marker perfusion technique, jejunal absorption rates of equimolar amounts of glycine in the form of free glycine (100 mM) and its dipeptide, glycylglycine (50 mM), were investigated in five healthy human volunteers and five patients with tropical sprue, before and after 6 months of treatment with folic acid (1 mg daily), vitamin B_{12} (1000 ug I.M. monthly) and oxytetracycline (250 mg twice daily). The absorption rates of both free glycine and glycylglycine were markedly reduced in the sprue patients, the reduction being more severe for free glycine than for glycylglycine. In four out of the five patients, the glycine absorption rates were significantly greater from the test solution containing glycylglycine than from that containing an equimolar amount of glycine in the free form. After 6 months of treatment all the tropical sprue patients had a normal absorption of glycylglycine while free glycine .absorption remained subnormal. The present studies indicate that dipeptide absorption is superior to that of the free amino acid even when the membrane transport is markedly reduced. Furthermore, the studies conducted in the untreated and treated tropical sprue patients demonstrate that recovery of dipeptide absorption is more rapid and consistent than that of the free amino acid.

HALLAZGOS RADIOLOGICOS EN LA DISPLASIA OCCIPITO-FACIAL-CERVICO-TORACICO-ABDOMINO-DIGITAL

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En 1973 delinitamos los caracteres clínicos y radiológicos específicos que permiten identificar esta condición hereditaria que es más frecuente en puertorriqueños. Es una condición autosómica recesiva, letal en la primera infancia, cuyo diagnóstico puede hacerse en el momento del nacimiento por sus hallazgos radiológicos, permitiendo diferenciarla de condiciones parecidas no letales.

La displasia OFCTAD se caracteriza por enanismo de tronco corto y deforme, occipucio prominente, dolicocefalia, frente ancha y despejada, inclinación palpebral mongoloide, puente nasal ancho, fases nasales intevértidas, piltro alargado, boca en carpa, cuello corto con inserción baja del pelo, cifosis o cifoescoliosis, imágen radiológicas de tórax características (en cangrejo) con hemivertebras, fusión de costillas, etc., abdomen prominente con laxitud de musculatura abdominal, extremidades aparentemente alargadas en relación al tronco, dedos alargados, camptodactilia y sindactilia parcial entre otros. Al presente hemos observado la condición en más de 20 casos.

NUTRITIONAL STATUS OF A CHRONIC ALCOHOLIC POPULATION IN PUERTO RICO

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Hematological and various nutritional parameters were assessed in 75 chronic alcoholics admitted to the Alcoholism Unit of the Department of Addiction Services. Of these, 68 (91 percent) were males and 7 (9 percent) were females. Anemia, defined as hematocrit levels below 40 percent for males and 37 percent for females, was present in 28 percent. Percent transferin saturation $<$ 20 percent was present in

41 percent, serum folate levels < 5 ug/L in 33 percent. serum B_{12} levels < 150 ng/L in 1 percent, and serum vitamin E levels < 0.6 mg/100 ml in 34 percent.

The most likely reason for the apparent iron deficiency in the subjects studied is overt and/or occult gastrointestinal bleeding; no history of frequent donations at commercial blood banks was obtained. The prevalence of low serum folate levels observed is comparable to that reported in other studies and probably secondary to a low dietary folate intake. Serum vitamin B_{12} levels were normal in all but one subject. The very high prevalence of low serum vitamin E levels has not been, to our knowledge, reported previously. Intestinal malabsorption of the fat soluble vitamins in chronic alcoholics could account for this finding. Data on the subjects' dietary intake of nutrients and alcohol will be presented.

SINDROME DE KOCHER-DEBRE-SEMELAIGNE: INFORME DE DOS CASOS

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El hipotiroidismo asociado con pseudohipertrofia muscular dando una apariencia atlética marcada o Herculea es extremadamente raro. La entidad ha sido informada en la literatura mundial en alrededor de 36 casos, siendo la mayor parte de ellos de origen asiático. La condición lleva el nombre de Kocher quien primero encontró la asociación de hipotiroidismo o hipertrofia muscular y de Debré y Sémélaigne quienes delimitaron la enfermedad.

Recientemente evaluamos dos cretinos nacidos de padres consanguíneos, quienes a los 22 y 27 años de edad presentan, además de los caracteres clásicos del hipotiroidismo congénito, desarrollo sexual completo y pseudohipertrofia muscular.

STUB TOE ASSOCIATED WITH PECULIAR FACIES, DIGITAL ANOMALIES AND GROWTH RETARDATION. A NEW SYNDROME.

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Over 20 patients have been evaluated who present sufficient clinical characteristics that suggest a previously undescribed, autosomal dominant condition. All the subjects present specific facial characteristics (slight frontal bossing, sparce eyebrows, prominent periorbital fat, elongated philtrum, horizontal position ofmouth with thin upper and broad lower lips, mild retrognatia and prominent ears with overfolded helix), long neck and square shoulders, short carpal area, slightinterdigital webbing, overriding (horse saddle) scrotum in males, short, broad, and externally curved big toe, mild to moderate spoon nails on toes, partial (cutaneous) syndactily on toes 2-3 and 4, normal mental development, delayed puberty and growth. Chromosome studies as well as thyroid function, human growth hormone, serum and urinary aminoacids have been normal. Sporadic cases as well as the suggestion of autosomal dominant transmission with variable penetrance have been observed in over 10 families.

STEROIDS AND ANTIBIOTICS PROTECT RAT FROM EXPERIMENTAL BOWEL ISCHEMIA

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Acute intestinal ischemia is fraught with a very high mortality because of pitfalls in diagnosis and treatment. Cellular damage, loss of cellular integrity, loss of the mucosal barrier, and the various types of shock account for this high mortality. Our previous experience with protection of ischemic organs and tissues led us to investigate the effect of steroids and antibiotics in this condition.

103 ramdom-bred rats weighing between 180-300 gms were anesthesized and subjected to superior mesenteric artery ligation for a period of one and one half hour. Either normal saline or methylprednisolone (40 mg/kg), ampicillin (12.5 mg/kg), diphenylhydantoin (10 mg/kg), or chlorpheniramine (5 mg/kg) were injected with a No. 30 gauge needle into the inferior vena cava either before or after ischemia, alone or in various combinations. After release of ischemia

the animals were observed for behaviour and survival. Survival occurred only in the methylprednisolone treated groups and especially when combined with ampicillin. In this group survival improved from 0 percent to 50 percent ($p < .05$ to $p < .001$). Behaviour in survivors was normal. Autopsy on survivors showed no abnormality, whereas non-survivors showed hemorrhagic enteritis.

Methylprednisolone combined with suitable antibiotics may be a valuable adjunct in the treatment of intestinal ischemia, as well as during temporary interruptions of superior mesenteric artery flow.

THE SURGICAL TREATMENT FOR HYPERPLASTIC RHINITIS VIA THE PTERYGOMAXILLARY FOSSA APPROACH. A STUDY OF ELEVEN CASES.

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The terms "hyperplastic rhinitis" refer to that condition of the nose characterized by hypersecretion and tissue hyperplasia. We know that etiologically it may be caused by atopic- histamine mediated factors and/or neuro-endocrine - vasomotor reaction. It is only in those severe Chronic, intractable cases that I recommend a more aggressive treatment. The pterygomaxillary fossa approach has been used for many years with success for internal maxillary artery ligation in cases of severe epistaxis; Vidian neurectomies for Vasomotor rhinitis and sphenopalatine ganglionectomies.

Eleven patients with Chronic hyperplastic rhinitis have been treated by this method, in our own media. The results are excellent and compare well with other data. The study is documented with several color microfilms obtained during the surgical procedure.

THE IMMUNOLOGIC EFFECT OF FAT ENRICHED DIETS IN MICE.

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For many years it has been known that fat enriched diets are associated with a high incidence of cancer. There is evidence that this may be due to changes in the hormonal milieu and to a co-carcinogenic effect. We wanted to see whether an immunologic effect was also operative.

Close to 120 mice of various strains were fed with Corn Oil (Mazola) and fatty acids (oleic or linoleic) since birth. Skin grafts between DBA/2 J and Balb/C, and between C57BL 6/J and C57Br survived longer in animals fed with fat-enriched diets than in controls. 6C3HED and dbrB tumors transplanted into C57Br and Balb/C mice also survived longer in groups fed with corn oil than with regular diets. Both set of experiments were statistically significant between $p < .05$ - $p < .003$. In vitro experiments were done as follows: PHA stimulation of lymphocytes from fat-enriched diets produced a less vigorous MIF response than control animals.

Fat diets produce a decrease in immunologic reactivity in mice. This may be a factor contributing to the high incidence of cancer in animals on a high fat diet. We postulate an alteration in the lipid content of the lymphocyte membrane with changes in its surface-modulation properties.

THYROTOXIC GRAVE'S DISEASE WITH NORMAL FUNCTION STUDIES

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A 32-year old male was recently investigated and thoroughly studied because of unequivocal clinical evidence of hyperthyroidism. He also had atrial fibrillation with a very rapid ventricular rate. Thyroid function tests were normal. Total and free thyroxine and serum triodothyronine (measured by radioimmunoassay), radioactive iodine uptake, T 3 resin uptake and PBI were all normal. There were no abnormalities in binding globulins and no clinical or laboratory evidence of thyroiditis. Serum LATS (long acting thyroid stimulator) was markedly elevated while serum TSH (thyroid stimulating hormone) was undetectable (both also measured by the radioimmunoassay method).

Reversal to sinus rhythm and disappearance of signs and symptoms of thyrotoxicosis was obtained after

treatment with propylthiouracil. The physiology of thyroid hormone metabolism and possible ethiopathogenic mechanisms will be the subject of the discussion in this interesting and unusual case.

TRATAMIENTO QUIRURGICO DEL SINDROME DE FREY MEDIANTE LA NEURECTOMIA TIMPANICA.

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Se describe el síndrome de Frey como una de las complicaciones más frecuentes de la parotidectomía, manifestándose por enrojecimiento y sudoración en el área anatómica de la glándula parótida, durante la masticación.

Su etiología, se relaciona con la regeneración aberrante de las fibras parasimpaticas destinadas a la glándula, que una vez seccionadas en el transcurso de la intervención, llegan a las glándulas sudoriparas de la piel, éstas últimas primariamente de inervación simpática.

El objetivo de esta comunicación es hacer una revisión de la literatura, investigar la incidencia en nuestro medio y la presentación de un caso tratado con éxito.

CLINICAL, ELECTROCARDIOGRAPHIC AND ANGIOGRAPHIC FINDINGS IN PATIENTS WITH CORONARY ARTERY ANEURYSMS

Juan M. Aranda, MD, Benjamín Befeler, MD, from the Veterans Administration Hospital, University of Miami School of Medicine.

Coronary artery aneurysms (CAA) were demonstrated angiographically in 11 out of 1176 patients referred for cardiac catheterization. Seven patients had angina pectoris, 3 presented with congestive heart failure and 1 had angina pectoris and congestive heart failiue. Seven patients had diffuse CAA, 4 had saccular aneurysms, and 1 had both. The right coronary artery was involved in 10 patients, the circumflex in 7 and the left anterior descending in 3. Left ventricular dysfunction was documented in all patients reported. Three patients did not have coronary obstructive lesions, but exhibited segmental left ventricular dysfunction, corresponding to the area of CAA. Although severe atherosclerosis was documented in all of the patients reported, eight patients had adequate distal run-off and were considered to be candidates for myocardial revascularization and/or left ventricular aneurysmectomy. Three other patients were treated medically. The patients were followed up from 6 to 46 months (average 27 months). One patient died of severe gastrointestinal bleeding 6 months after the operative procedure. Similar lesions were found in the mesenteric arterial system. Ten patients are alive, seven have noted a significant clinical improvement.

Coronary artery aneurysms in patients with angina pectoris appear to be a well defined subgroup of patients with coronary atherosclerosis. The aneurysms can produce ischemia and segmental left ventricular dysfunction with or without coronary obstructive lesions. Aorto-coronary bypass surgery can be accomplished successfully in those patients with adequate distal run-off.

CANDIDA TROPICALIS ARTHRITIS: A RARE ENTITY.

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A 70-year old retired carpenter was admitted to the University Hospital with septic arthritis. *Staphylococcus epidermidis* was grown from the knee. The orthopedic surgery service performed an open drainage procedure with continuous irrigation and removed a torn meniscus. After seven days of continuous local antibiotic irrigation and systemic antibiotics the involved knee was found to be hot and swollen. The patient developed fever, antibiotics were changed to gentamicin plus methicillin. Gram stain of the joint aspirate revealed yeast cells, *Candida tropicalis* on culture. There was no evidence of dissemination. The patient was started on amphotericin B. After receiving 426 mg,, therapy was stopped due to de-

terioration of renal function. Two days later there was a flare up of the knee. A synovial biopsy revealed yeast cells but joint fluid culture was negative for Candida. He was restarted on alternate day amphotericin B with mannitol. The knee inflammation subsided and there is no evidence for redness, tenderness or fluid accumulation. The patient is ambulating well. We want to share our experience in the treatment of fungal arthritis and to review the pathogenicity of Candida species and fungal arthritis. Specially when this is the second report of joint infection with *Candida tropicalis* in the English literature.

DENGUE HEMORRHAGIC FEVER: A CASE REPORT

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Dengue is endemic in PR and the Caribbean. Dengue with hemorrhagic manifestations is rare in the Western Hemisphere and not reported until recently in the Caribbean.. A male in his mid 40's, in good health had the sudden onset of fever, chills, headache, generalized malaise, body aches and anorexia. He was diagnosed as a "flu" like illness and treated with analgesics and antibiotics by his physician. After 48 hrs of therapy there was no improvement, and 2 days later developed a generalized petechial rash and bleeding from the gums. He was sent to VA Hospital where he was found acutely ill with normal vital signsand low grade fever. There was a generalized petechial rash involving skin and mucous membranes, bleeding gums, large echymosis over right shoulder and scleral icterus. There was leukopenia,t thrombocytopenia, normal hemoglobin and hematocrit. Bone marrow was compatible with immune thrombocytopenia. On the second hospital day he experienced tarry stools. He was treated with corticosteroids and platelet transfusions. Clinical response was excellent in two days, corticosteroids were tappered down over a 6 week period. Diagnosis of dengue was confirmed by serologic rise against dengue 2 virus by complement fixation and hemagglutination inhibition test. Immunoglobulin and complement levels remained unaltered during the illness. We will discuss the pathogenesis, clinical presentation and management of an apparent uncommon illness, dengue with hemorrhagic manifestations.

FASCIOLASIS HUMANA: PRIMER REPORTE EN LA LITERATURA INSULAR.

Edrick López-Enrique, MD, Hamid Galib-Frangie, MD, Carlos Ramírez Ronda, MD, Escuela de Medicina, Universidad de Puerto Rico, Departamento de Medicina Interna, Hospital Universitario, Río Piedras, Puerto Rico.

Se presenta el primer caso de infestación por *Fasciola hepática* adquirida en Puerto Rico. La presencia de ganado vacuno infectado, existencia del molusco Lymnea en nuestro suelo, el clima tropical y húmedo y la reciente proliferación de huertos caseros hacen de nuestro ambiente una condición ideal para la promulgación de esta entidad clínica. La presentación clínica de esta entidad es no específica con fiebre, malestar general, apetito pobre y hepatomegalia. Algunos casos pueden presentarse con ictericia. Data epidemiológica que ayuda en el diagnóstico es un historial de ingerir vegetales crudos, cultivados en terrenos húmedos. El diagnóstico de esta condición se hace por la presencia de huevos del verme en la excreta del paciente. Este diagnóstico se corrobora con la mesura de títulos de anticuerpo contra *Fasciola hepática* por el método de contrainmunoelectroforesis. El tratamiento es con bithional o emetina y debe de llevarse a cabo en un centro especializado. El mejor de los tratamientos es prevención. Queremos alertar a la comunidad médica del país sobre el problema de fasciolasis humana. Presentaremos la metodología y técnicas para la prevención, reconocimiento, diagnóstico y manejo de la entidad clínica.

HYPERLIPOPROTEINEMIC TYPES AMONG PUERTO RICANS: A FINAL REPORT.

Marta Cancio, PhD, and José M. León, BS, MT, General Medical Research Laboratories, VA Hospital, San Juan, Puerto Rico.

This report summarizes the results of a study on hyperlipoproteinemic Puerto Rican subjects performed during an eight years period. Classification in types was done according to the World Health Organization. Distribution of cases by type was: 5 Type I, 258 Type IIa, 198 Type IIb, 186 Type IV, and 76 Type V. Type I were all children of Caucasian race; 4 females, 1 male. Type IIa were mostly in their fifties, while Types IIb, IV and V peaked in number in their forties. Over 90 percent of cases in all types except Type V were Caucasian; in Types IIa, IIb, IV and V close to 90 percent or over of cases were male. In type IV 78 percent were obese and 67 percent were diabetic. These conditions were also high (over 60 percent) in Type V. CVD was high (over 60 percent) in Types IIa and IIb. Over 60 percent of the cases of all types were from the Northern region of Puerto Rico.

PHARYNGEAL FLORA IN MALE ALCOHOLIC PATIENTS: A PROSPECTIVE STUDY.

Zelma Fuxench-López, MSIV, Minerva Nevárez-Carrasco, BSMT., C. Ramírez Ronda, MD, FACP, Departments of Research and Medicine, VA Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

The occurrence of pneumonia caused by gram negative bacilli (GNB) is increased in the alcoholic patient (AP). In order to get insight into the factors that might contribute to this, we designed a prospective study of pharyngeal flora in AP and in a control group (CG). Ambulatory male VA patients were randomly selected and interviewed using a standard questionnaire. Patients that met the National Council of Alcoholism Criteria were in the AP group. Twenty eight met the criteria. A CG matched for age and socioeconomic status composed of 23 patients was also studied. Patients with hospitalization within the last 6 months were excluded. All patients had liver function tests and pharyngeal cultures. Pharyngeal flora was studied using quantitative aerobic cultures of saline gargle. Identification was carried by standard microbiological methods. One or more GNB were isolated from 64 percent of the AP, while in only 9 percent of the CG. In 6/18 AP GNB were found in high numbers, and 3/21 isolates in AP were multiple isolates. The rest of the patients had low colonization rates. The most frequent isolate was Klebsiella pneumonia 48 percent and the Klebsiella-Enterobacter group accounted for 83 percent of the isolates. There was no difference in gram positive and fungal pharyngeal flora between the groups. The data suggests that: 1) the increased incidence of Klebsiella-Enterobacter pneumonia among alcoholics could relate to the increased numbers of these organisms in the pharyngeal flora. 2) The high prevalence of GNB in pharyngeal flora of ambulatory AP without pneumonia indicates that sputum and throat cultures obtained from AP are not a reliable means for diagnosing GNB pneumonia.

Q FEVER IN PR: A CASE REPORT

Carlos León Valiente, MD, Carlos Ramírez Ronda, MD., Migdalia González, MD and Sergio Sarita-Valdés, MD., Depts. of Medicine and Pathology, VA Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

A female in her early 50's was in her usual health until the Fall 1975 when she developed SOB, orthopnea, cough, productive of yellow sputum and anorexia. Was seen by her physician, treated with antibiotics without improvement and referred to the University Hospital. On admission she was tachypneic and acutely ill, low grade fever was present. Physical examination was compatible with pneumonic findings, and occasional wheezes. Chest x-ray showed bilateral diffuse interstitial infiltrates. Pulmonary function studies revealed an obstructive pattern. She was given penicillin and gentamicin without improvement. Sputum, blood, urine and throat cultures grew no pathogens. CBC was normal including a WBC count of 10,700. SMA-12 was normal, PPD was negative X2. Upon review of history she denied exposure to birds, parrots, parakeets, there was no history of a similar illness in the family, nor earache. No history of exposure to TBC. During the summer of 1975 she visited Western USA and several cattle and sheep raising farms. An open lung biopsy was performed revealing an interstitial pneumonia, and small round coccobacilli on special stain compatible with rickettsiae. The diagnosis was confirmed by increase in serologic titers against Coxiella burnetti. Serologies for mycoplasma and psittacosis were negative. She was treated with tetracycline for 3 weeks with improvement and cure. We will discuss

the epidemiology, diagnosis and management of the patient with atypical pneumonia.

TETANUS ANTITOXIN LEVELS IN PUERTO RICAN MALES: A PRELIMINARY REPORT

Héctor F. Gorbea, MSIV, Rosa Lluberes, BSMT, and C. H. Ramírez Ronda, MD, FACP., Departments of Research and Medicine, VA Hospital and University of Puerto Rico School of Medicine, San Juan, P. R.

Tetanus is still a serious health problem in southern United States and in Puerto Rico. The attack rates in the USA are of 0.071/100,000 and the rates are higher in Puerto Rico. Tetanus occurs most frequent in elderly males and in the very young. In order to detect the level of protection against tetanus in Puerto Rico a prospective study was designed. A population of male VA patients and male University District Hospital (UDH) patients was interviewed and a standard questionnaire filled. Five groups of patients were studied, World War I veterans, Group I (GI), World War II veterans, Group II (GII), Korean Conflict veterans, Group III (GIII), Vietnam veterans, Group IV (GIV), and UDH patients, Group V (GV).

Tetanus antitoxin (TAT) levels were measured by passive hemagglutination assay using sensitized sheep RBC's. All tests were run with an individual control. TAT protection was defined as 0.01 antitoxin unit per ml or more. The mean age of the groups is as follows: GI-84, GII-58, GIII-44, GIV-28, GV-36. There was protective TAT levels in all groups except GI. The mean antitoxin levels in antitoxin units per ml were GI-0, GII-0.2, GIII-0.22, GIV-0.13, GV-0.20. The older the patients the lower the TAT level.

The preliminary data shows that PR males between the ages of 20-65 have adequate TAT levels, that elderly males ages 75 and up have no protection and should be immunized. Further conclusions will be drawn when the sample studied is increased and females, newborns and children are included.

USE OF COUNTERELECTROPHORESIS FOR THE IMMUNODIAGNOSIS OF *FASCIOLA HEPATICA*.

Noemí Santiago de Weil and Goerge V. Hillyer, Department of Biology, University of Puerto Rico, Río Piedras, P. R. 00931

Counterelectrophoresis (CEP) has been demonstrated to be a rapid, accurate test for the immunodiagnosis of human trichinosis (Despommier, et al, 1974, *Amer. J. Trop. Med. & Hyg.*, 23: 41-44) and amoebasis (Sepúlveda, et al, 1971, *Arch. Invest. Med.*, 2: 263-268). Studies in our laboratory have shown CEP suitable for detecting fasciolasis infections in rabbits, mice, hamsters, rats and humans (Hillyer, 1975, *J. Parasit.*, 61: 557-559). In addition, chemotherapeutic success has been predicted by CEP in rabbits with fascioliasis (Hillyer and del Llano de Díaz, 1976, *Amer. J. Trop. Med. & Hyg.*, 25: 307-311). In studies to detect immunological changes following chemotherapy in rats with fascioliasis we found that the serum of a very large proportion of normal rats gave a sharp line of precipitation with *F. hepatica* adult worm extract by CEP thus invalidating this test system. In order to eliminate this problem the crude antigen was fractioned using Sephadex G-200. Of the four peaks eluted, the crest and descending fractions of peak II and all of peak III were pooled and sued as an antigen for CEP tests. This partially purified antigen, when used in CEP, showed reactivity with sera from infected rats but not with normal rat sera. In addition, sera from mice with schistosomiasis did not react with this antigen, eliminating a problem regarding specificity when using the crude *F. hepatica* extract.

This partially purified antigen was also tested against 37 sera from patients with fascioliasis, kindly donated by André Capron in France, having demonstrable antibodies to the parasite by immunoelectrophoresis, immunofluorescence and hemagglutination. When tested by CEP all of these sera gave sharp lines of precipitation with *F. hepatica* adult worm extract. However, the crude antigen had extensive cross-reactivity with sera from humans with schistosomiasis, trichinosis, amoebiasis and cysticercosis. The use of the partially purified antigen obtained by chromatography with Sephadex G-200 eliminates most of this cross-reactivity and permits the use of CEP for the immunodiagnosis of fascioliasis. Our present efforts include adapting this test for the immunodiagnosis of schistosomiasis. These studies were supported by NIH Grant No. RR-8102.

U. S. MEDICAL SCHOOLS ENROLL RECORD TOTAL OF STUDENTS

CHICAGO– A total of 57,236 medical students were enrolled in 116 medical schools across the country this fall, including 15,349 first-year students – a record number, the American Medical Association reported.

The rate of increase of enrollment tapered off this fall, increasing only slightly over last year. The nation's medical school enrollments are leveling off, at least temporarily, the AMA said. Total enrollment this fall is about 9.7 percent greater than last year's the first-year enrollment is about 9.4 percent greater than last year.

This year two new medical schools accepted their charter classes: Wright State University College of Medicine, Dayton, Ohio, and the University of Health Sciences of the Uniformed Services, in Bethesda, Md.

Women students accounted for 20.4 percent of total enrollment in the medical schools this year, about the same percentage as last year. Minority students represented 8.2 percent of total enrollment, and 9.3 percent of the freshman class, about the same as last year.

The preliminary enrollment figures were gathered in the annual survey of medical schools conducted jointly by the AMA and the Association of American Medical Colleges.

This fall's first-year enrollment was 24 percent greater than five years ago, and total enrollment is nearly 29 percent greater than five years ago.

INTERNSHIP IS CRUEL JOKE, YOUNG DOCTOR CHARGES

CHICAGO– The difficult grind of the medical internship is castigated by a young doctor in an opinion article in the Sept. 13 issue of American Medical News, the newspaper for physicians of the American Medical Association.

"Internship is a cruel joke to play on an eager and unsuspecting young doctor on his first venture into the world," declares Deborah Rich, M.D. Dr. Rich graduated from George Washington Medical School, Washington, D. C., in 1975, recently completed internship in Providence, R. I., and is presently serving a residency in internal medicine at the Washington Hospital Center, Washington, D. C.

"Doctors spend their lives in search of the perfect sleep," declares Dr. Rich.

"Interns are ineligible for the pursuit, being left instead to perform the household chores (answering phones, collecting laboratory and X-ray results, writing progress notes and orders, performing procedures), to serve as the resident diplomats for the patients and their families, nursing staff, social service, private doctors, and other hospital physicians."

Dr. Rich continues:

"An internship guarantess no chance or space to be alone; no time to go to the bathroom or eat leisurely; no opportunity to unwind or reflect, to laugh unself-consciously or cry alone. During this time most relationships deteriorate, poisoned by hospital overkill.

"By the end of the year I hated my patients, their families, my residents, my attendings, anyone who told me he or she wanted to go to medical school. Every phone call became a potential catastrophe. I wondered how much longer I could continue to fool my patients about enjoying my new career as a doctor."

Another article in the same issue of the newspaper describes how two young doctors have united to serve one internship, each working on alternate months. This will extend the training period to two years for both, instead of one year.

They are Naomi Kistin, M. D., and Ron Sable, M. D., who are sharing one intern's slot at Chicago's Cook County Hospital. They also share the one salary of $12,000 a year. Dr. Sable, a one time Vietnam corpsman, is a graduate of U. of Missouri Medical School. Dr. Kistin attended U. of Illinois Medical School.

On their alternate months off, each doctor has time for study and reflection and to catch up on sleep, they report. Both are well pleased with their shared internship.

TESTS OF UNBORN CHILD REVEAL POTENTIAL DEFECTS

CHICAGO– All pregnant women past the age of 35 should be offered a test to determine whether their child will be normal, declares a research report in the Sept. 27 Journal of the American Medical Association.

The older mothers have an increased risk of giving birth to Mongoloid infants, the report points out. The test also should be given to expectant mothers of all ages who are Rh-negative, diabetic, have high blood pressure, or have a family history of defective children.

The test, known as amniocentesis, is a highly accurate and

safe procedure, for both the mother and the unborn child, says the report from the National Institute of Child and Human Development, Bethesda, Md., following a five-year study.

Amniocentesis means the extraction and analysis of fluid from the sac surrounding the baby inside the pregnant woman. It can predict many potential abnormalities. It also can detect the sex of the baby some months before birth.

Of the 1,040 women undergoing the test in the NICHD study, more than 95 percent were reassured of no abnormality in the fetus and their pregnancies continued, the report says.

"Amniocentesis served to provide reassurance, assistance in having normal children, and, in numerous instances, avoidance of abortion," the NICHD says.

Some 39 of the women learned from the tests that their child would be seriously deformed, and elected to have abortions.

There was no indication that amniocentesis injured either the mother or the unborn child, the report says. Diagnostic accuracy was 99.4 percent.

DOCTORS WARNED OR RISK OF DROPPING LIABILITY INSURANCE

CHICAGO– The medical doctor who risks "going bare" – practicing without malpractice insurance – runs the risk of complete financial ruin, says a report on the Sept. 27 issue of the Impact section of American Medical News, the weekly newspaper for physicians of the American Medical Association.

A recent survey by Impact found that 35 percent of physician respondents said they are thinking of dropping malpractice coverage, while 13 percent say they are currently without any malpractice insurance. The insurance rates have skyrocketed in recent years.

"Going bare" is a good idea "only for the very few tough minded individuals who can live with the possibility of losing everything they've acquired in a lifetime of practice, plus a good chunk of their future earnings," W. Fred Mangan, head of a Michigan management consultant firm, told the newspaper.

If the doctor drops his malpractice insurance, the only way he can keep from losing his assets in a future malpractice action is not to have any assets to lose. He has to give them away. Mangan pointed out. And the give-away must be complete and irrevocable, with the doctor retaining no control over the assets.

Some physicians have considered putting all property in their wife's name, but, says Mangan, the chances of losing everything through divorce are much greater than any risk from malpractice. He points out that the American divorce rate is now 43 percent of marriages.

If the doctor has no insurance and few assets to pay a malpractice judgment, the plaintiff's lawyer likely will obtain a court order attaching future earnings. Medicare, Medicaid, Blue Shield and insurance companies could be ordered to send checks to the plaintiff rather than the doctor, the doctor's bank accounts could be attached, and the plaintiff even could have someone sit in the doctor's office and collect all money paid by patients.

The doctor who "goes bare" may end up exactly that – bare, the consultant declared.

MALPRACTICE RATES HURTING PATIENTS

CHICAGO– Cost of physicians' malpractice insurance is hitting the patient where it hurts – in the pocketbook.

Patients paid an estimated $1.24 for malpractice insurance each time they visited a doctor in 1975. That amount was about 8.1 percent of the full amount the patient paid for the visit, according to preliminary estimates of the American Medical Association. The impact on the patient this year is even greater, the AMA said, because malpractice insurance rates are still on the upswing.

In 1973, a patient paid an estimated average of 30 cents per doctor visit for malpractice insurance, or about 2.4 percent of the full price of the visit.

AMA's estimates are based partly on its own survey of physicians and partly on data from Federal agencies. The cost of his malpractice premium is considered to be a business expense of a physician, a component of the fee he charges.

Physicians paid an average of $610 for malpractice insurance in 1968 and $1,905 in 1973, the AMA's survey of doctors revealed. Since then, according to a government survey of the insurance industry, the premiums went up another 84 percent in 1974 and 125 percent in 1975. The AMA used those percentage increases to estimate the average payment per doctor in 1975 for malpractice insurance, $7,887.

All told, doctors' business expenses (including their malpractice insurance rates) have been rising substantially faster than increases in doctors' fees. During the eight years 1966-1974, doctors' business costs per patient were rising at an 8.3 percent per year rate, the AMA study says. At the same time, according to the Consumer Price Index, doctor's fees went up at 6.2 percent average annual rate.

"When Federal controls on physician fees were dropped in 1974, we asked physicians to do their best to hold the line," commented AMA executive vice president James H. Sammons, M. D. "Physician fees have not risen as rapidly as their costs. But no one can reasonably expect doctors to absorb the sometimes horrendous impact of increased malpractice insurance premiums."

MEMO FROM THE AMA PUBLIC AFFAIRS DIVISION

TO: Executive Directors - State Medical Associations

FROM: Definition of Medical Rehabilitation Services

The AMA House of Delegates at the 1976 Annual Convention adopted the definition below, and a resolve that the definition be distributed to "state agencies and state boards of medical examiners." The AMA is sending this definition to the state boards, but we ask that you advise the appropriate state agencies of this action.

For your information, this definition was unanimously approved by the AMA Interspecialty Council prior to the action by the House of Delegates.

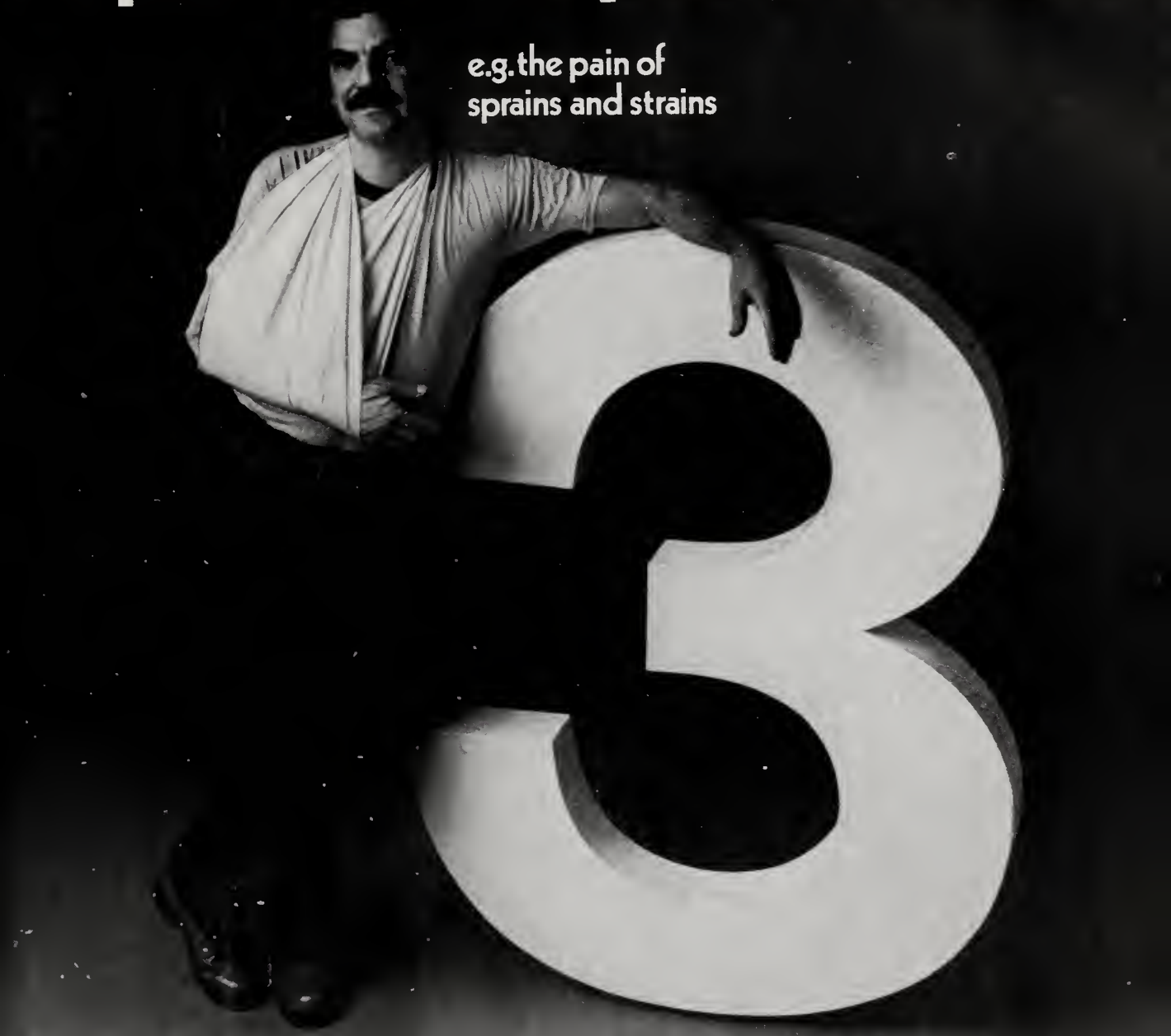
DEFINITION OF MEDICAL REHABILITATION SERVICES
(Resolution 1, A-76)

"Medical Rehabilitation Services are defined as a coordinated multidisciplinary approach to disability under a qualified physician who directs a plan of management of one or more of the categories of chronic disabling diseases or injuries, specifying realistic goals for maximum recovery. That approach may include, if required, several or all of the following services: skilled rehabilitation nursing care, physical therapy, occupational therapy, speech therapy and audiology services, prosthetic and orthotic devices and services, social, recreational and psychological services."

ANUNCIO

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Breast self-examination:

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item:	**Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.**
item:	**Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, *fewer than 1 in 5* women practice BSE, and *only half* have an annual breast examination by a physician.**
item:	**Only 35% of all women polled reported that a *physician* had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.**
item:	***But*, among women who received personal instruction from their physicians, the overwhelming majority *(92%)* practiced BSE during the preceding year.**

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE.

The American Cancer Society gives major emphasis to breast cancer through research and a vast array of public educational materials, designed to give women life-saving information about the disease. Our latest approach is via a pioneering television film starring Jennifer O'Neill, "Breast Cancer: Where We Are." Where we *will* be in a few years will certainly hinge on our joint efforts.

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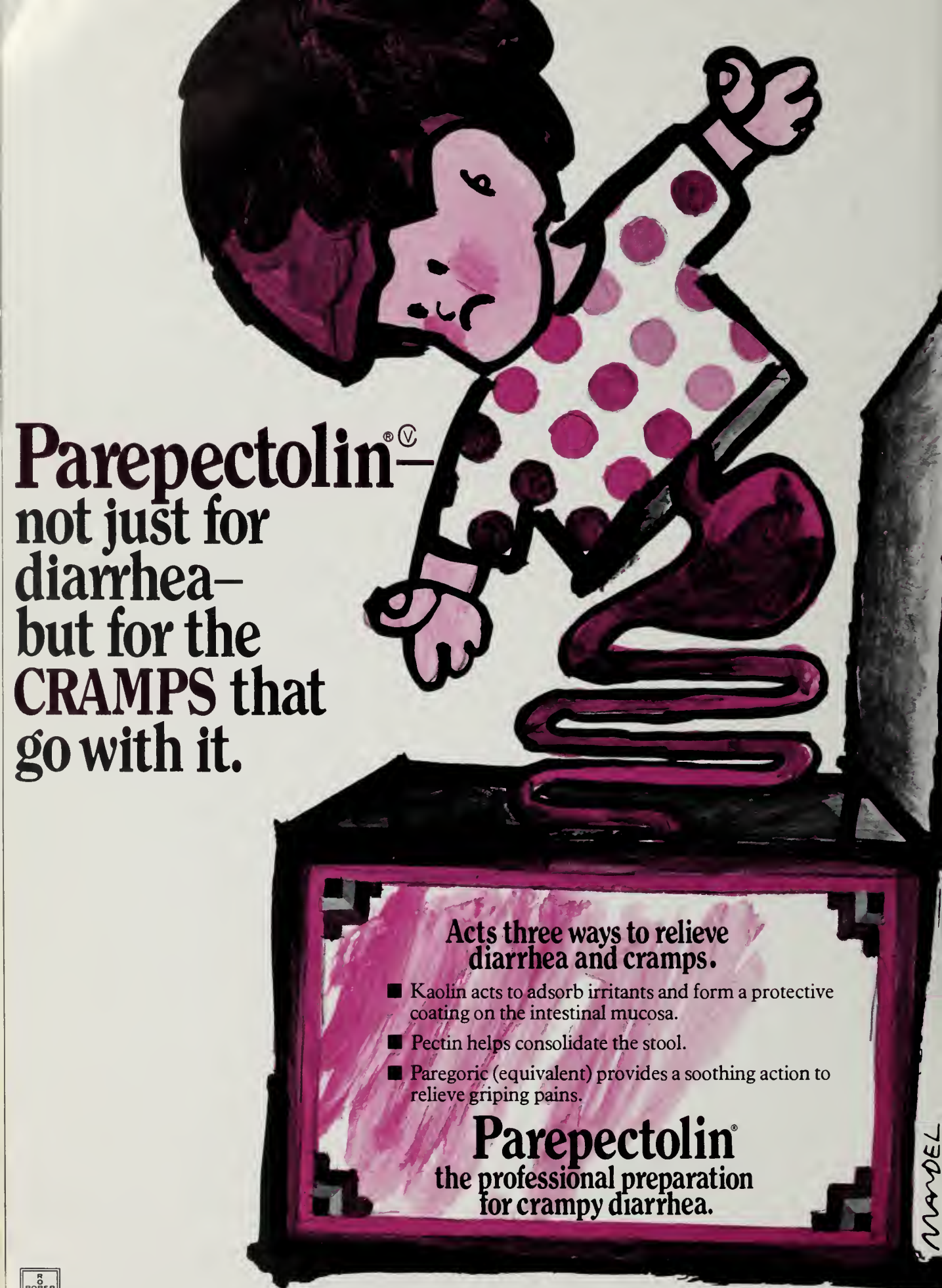
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BRIEF SUMMARY
Indications: Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone; routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May be additive or potentiative of the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Usage in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in cord blood and breast milk. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis; dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia; purpura, photosensitivity, rash, urticaria, necrotizing angiitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg. (white, scored) and 50 mg. (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6.



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CONTRAINDICATIONS: Anuria, oliguria, or significant impairment of renal function; infants under one month; pregnant patients at term; known hypersensitivity

WARNINGS: May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. (Such patients should be closely observed while receiving nitrofurantoin.) Discontinue the drug at any sign of hemolysis.
Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to Pseudomonas. Safety not established during pregnancy and lactation, should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.

PRECAUTIONS: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence

ADVERSE REACTIONS: Gastrointestinal Reactions—Anorexia, nausea, emesis are the most frequent reactions; less frequently, abdominal pain and diarrhea, rarely, hepatitis. This dose-related toxicity reaction can be minimized by reduction of dosage, especially in the female patient.

Hypersensitivity Reactions—Pulmonary sensitivity reactions, which can be acute, subacute, or chronic. Acute reaction is commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on X-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and resolve with cessation of the drug therapy
Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation of the drug therapy.

Dermatologic Reactions—Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

Other Sensitivity Reactions—Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.

Hematologic Reactions—Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy

Neurological Reactions—Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

Miscellaneous Reactions—Transient alopecia

SUPPLIED: Macrodantin (nitrofurantoin macrocrystals) is available in opaque, yellow capsules of 100 mg (coded "Eaton 009") and in opaque, yellow and white capsules of 50 mg (coded "Eaton 008") in bottles of 30, 100, 500, and 1,000 capsules, and in opaque, white capsules of 25 mg (coded "Eaton 007") in bottles of 100 capsules. Macrodantin Capsules, 50 mg and 100 mg, are also available in hospital unit-dose packages, strip-packaged in boxes of 100.

Septra® vs Nit

Each tablet contains:
80 mg trimethoprim and 400 mg sulfamethoxazole

A new clinical

Efficacy: A draw.

By randomized assignment, 149 patients received two Septra tablets b.i.d. and 140 received one 100 mg capsule of nitrofurantoin macrocrystals q.i.d. for 14 days. Eight days after therapy ended, 94% of patients treated with Septra had a clear culture vs 90% of those treated with nitrofurantoin macrocrystals.[1]

Laboratory changes: A draw.

There was no significant difference in the incidence of laboratory changes except in one instance; a significantly larger proportion of patients on nitrofurantoin macrocrystals had decreased lymphocyte counts than did patients on Septra.[1] The significance of this change is not known. (For further details see page three of this advertisement.)

Clinical side effects: Advantage, Septra.

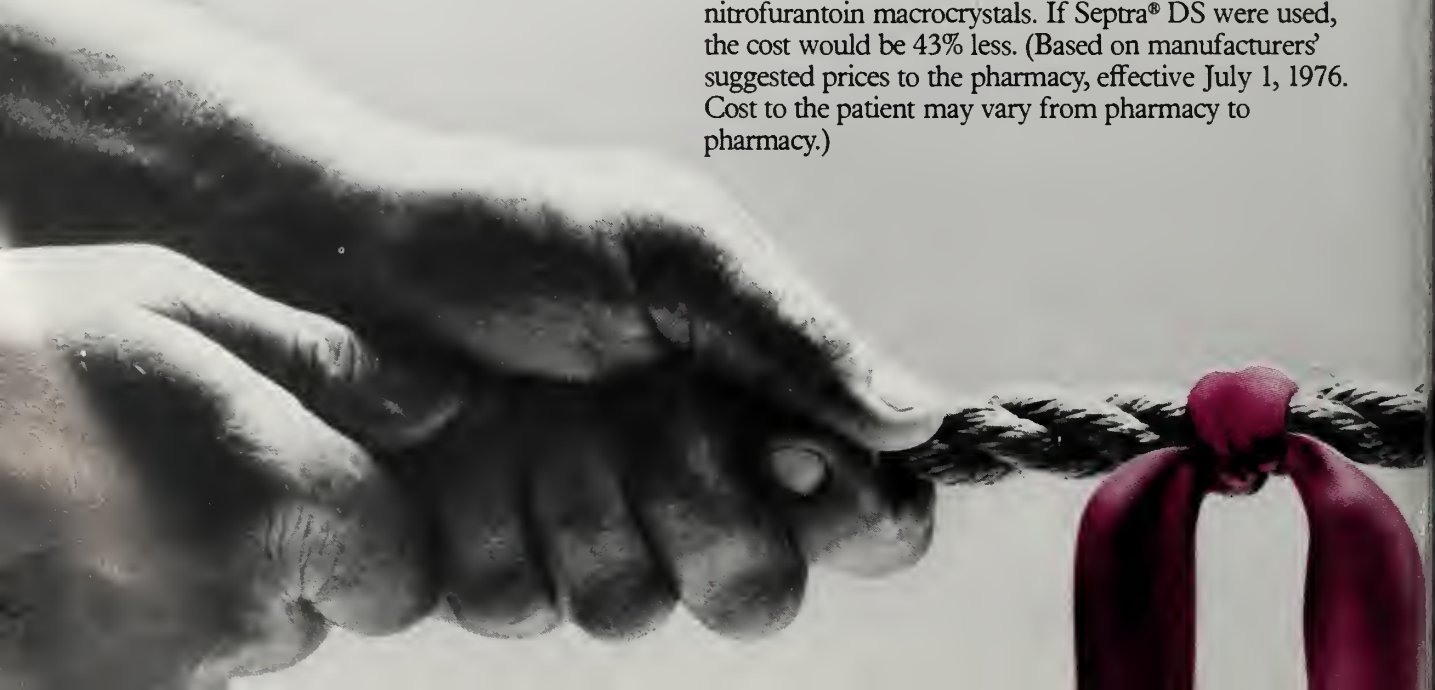
A significantly larger proportion of patients experienced side effects on nitrofurantoin macrocrystals (13%) than on Septra (6%).[1] (For further details, see chart on page three of this advertisement.)

Convenience: Advantage, Septra.

To maintain effective antibacterial activity, Septra is taken just twice a day, while nitrofurantoin macrocrystals are taken four times daily. The Septra dosage schedule offers obvious advantages in terms of patient convenience and compliance.

Cost: Advantage, Septra.

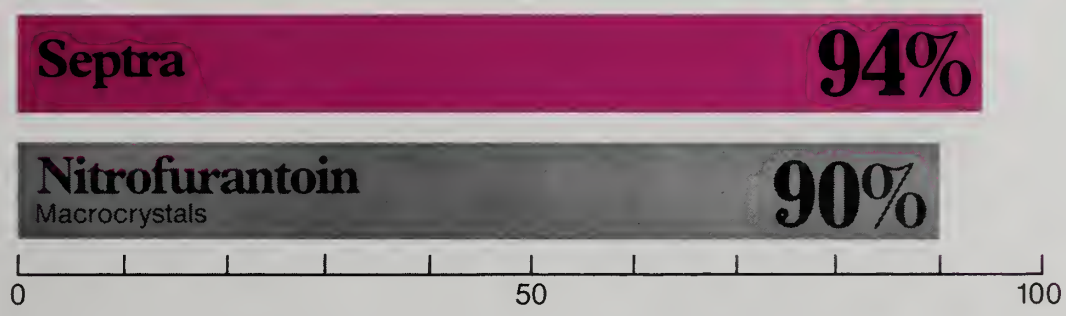
At the dosages used in this study, a course of therapy with Septra would cost 26% less than a course of nitrofurantoin macrocrystals. If Septra® DS were used, the cost would be 43% less. (Based on manufacturers' suggested prices to the pharmacy, effective July 1, 1976. Cost to the patient may vary from pharmacy to pharmacy.)



rofurantoin
Macrocrystals

confrontation

Results after 14-day course of therapy in 289 patients with recurrent urinary tract infections*[1]



% of patients with clear culture 8 days after therapy ended

*Due to susceptible strains of *E coli, Klebsiella, Enterobacter, Proteus mirabilis* and other *Proteus* species. Criterion for infection—100,000 or more organisms/ml urine. Criterion for "clear culture"—1,000 or fewer organisms/ml urine.

Septra® DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Double Strength Tablets.

The most economical form of Septra.



See next page for prescribing information.

Important clinical update on Septra—see previous pages.

Septra® vs Nitrofurantoin Macrocrystals

Each tablet contains:
80 mg trimethoprim and
400 mg sulfamethoxazole

Clinical side effects: Advantage, Septra.

Side effect	Frequency[1]	
	Septra	Nitrofurantoin macrocrystals
nausea	3	16
vomiting	1	9
anorexia	1	4
abdominal pain	—	2
diarrhea	—	4
headache	2	—
dizziness	—	1
diaphoresis	1	—
pruritus	2	1
vaginitis	1	—
maculopapular rash	1	1
rash	—	2
urticaria	2	—
	14	40

Note: All patients who originally entered the study described on previous pages were included in the evaluation for clinical side effects (192 patients received Septra, 191 received nitrofurantoin macrocrystals). Some patients experienced more than one side effect. See **Adverse Reactions** section below for other reactions that may be encountered.

Laboratory changes: A draw.

Type of change	Drug administered No. patients with change/total patients tested[1]	
	Septra	Nitrofurantoin macrocrystals
RBC ↓	14/141	14/141
Hemoglobin ↓	27/188	36/183
WBC ↑	3/188	3/183
" ↓	6/188	7/183
Bands ↑	3/183	3/176
" ↓	26/183	20/176
Hematocrit ↓	34/188	27/183
SGOT ↑	5/176	4/167
Basophils ↑	14/179	16/171
Neutrophils ↑	27/188	25/182
" ↓	3/188	6/182
Lymphocytes ↑	15/188	18/182
" ↓	11/188	21/182
Eosinophils ↑	14/179	8/177
Monocytes ↑	10/188	11/180
" ↓	23/188	23/180
Specific gravity ↑	1/187	—
" " ↓	—	1/177
Casts ↑	6/186	5/182
WBC/HPF ↑	9/190	13/185
RBC/HBF ↑	12/190	12/185
Bacteria ↑	9/189	11/183
" ↓	30/189	32/183
Crystals ↑	9/185	9/181

Note: Certain patients were not tested for some of the laboratory values listed above. Therefore, the chart specifies the total number of patients who completed the prescribed series of tests for each individual laboratory measurement.

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method *(Federal Register 37:* 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **At present, data are insufficient to recommend use in infants and children under 12.**

Precautions: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

Reference: 1. Data on file, Medical Department, Burroughs Wellcome Co.

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Hearing losses are among the most consistently neglected health problems. Many people with them won't even admit it to themselves, let alone others. A little encouragement may start them thinking about themselves more realistically.

That's why we're offering you the poster shown here. You can hang it on the wall or stand it on a small table. It comes with booklets called "As precious as sight" that give your patients some basic facts about auditory testing and hearing losses and how easy they are to correct in many cases.

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7.	SMITH, KLINE & FRENCH	ANNOUNCING
8.	SYNTEX LAB.	NEO-MULL-SOY
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Vol 68 Diciembre 1976 No. 12

Both often



Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium®
(diazepam) Ⓥ

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Volumen 68 Diciembre 1976 Número 12

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Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

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PORTADA: Hospital Universitario de Niños
(Cortesía Hospital Universitario de Niños)

NUESTRA PORTADA



FESTSCHRIFT

Honrando al Dr. Antonio Ortiz

***El Hospital Universitario** de Niños acabado de construir es la nueva sede del Departamento de **Pediatría** de nuestra Escuela de Medicina. En su diseño quedan grabadas las inquietudes, la filosofía y las convicciones del Dr. Antonio Ortiz como educador y pediatra completo.*

DEDICATORIA: HONRANDO AL DR. ANTONIO ORTIZ

José E. Sifontes, MD

If today we have a broader vision of our science than the men of 25 years ago, it is not because our sight is better but because we stand on their shoulders.

Luther Emmett Holt

Terminaba la década del '40; era la época en la que completaban su obra muchos de los primeros grandes de la pediatría mundial, entre ellos Heinrich Finkelstein, Adalbert Czerny, Isaac Arthur Abt, Isak Jundell, George Frederic Still, Frederic Poynton, Thomas Cooley, Joseph Brennemann, Oscar Menderson Schloss, Kenneth D. Blackfan, C. Anderson Aldrich y A. Graeme Mitchell. En Puerto Rico, muchos médicos interesados en la pediatría habían logrado notables aciertos, pero no había llegado hasta entonces la pediatría académica.

Fue en este momento cuando en el viejo Hospital Municipal de San Juan, el doctor Antonio Ortiz se dedicó a crear un servicio de pediatría acreditado por el "American Board of Pediatrics". Después de enfrentarse a extraordinarios obstáculos y limitaciones, organizó y creó el primer servicio de pediatría en Puerto Rico acreditado por el "Board of Pediatrics" para adiestramiento completo en la especialidad.

De ese programa de adiestramiento, que comenzó a fines de la década del '40, salieron muchos de los líderes de la pediatría de Puerto Rico y la mayor parte de los docentes de la Facultad de Pediatría de la Escuela de Medicina. Más tarde, comenzaron los programas de adiestramiento en las subespecialidades pediátricas que ofrecieron servicios pediátricos más modernos, de mejor calidad y muchas veces únicos en Puerto Rico. Surgieron importantes contribuciones científicas originales en diversos campos de la pediatría; las numerosas e importantes publicaciones de los miembros de la Facultad durante el período 1952-1972 son testigo de la productividad de estas dos décadas.

La insistencia contínua del Dr. Ortiz en la excelencia contribuyó a mejores servicios para los niños y al mejor adiestramiento de los médicos en formación. En el servicio de pediatría del Dr. Ortiz, se educaron cientos de estudiantes de medicina y el impacto de la excelencia alcanzó a todo Puerto Rico. En el 1967 se aprobó por el Secretario de Salud, Dr. Mario R. García Palmieri, la construcción del nuevo hospital de niños y el doctor Ortiz trabajó arduamente durante varios años en asesorar a los arquitectos sobre el diseño del mismo. En estas instalaciones quedaron reflejados el producto de la vasta experiencia del Dr. Ortiz y su gran preocupación por darle lo mejor al niño puertorriqueño. El Dr. Ortiz manifestó siempre gran preocupación por brindarle la mejor atención al niño más necesitado y desamparado. Insistió en que no se construyeran servicios por separado para indigentes y pudientes; que más bien el diseño de unas instalaciones de servicios de salud estuviera basado en las necesidades del paciente de acuerdo con el tipo y severidad de su afección.

El Dr. Antonio Ortiz nació en Maunabo, Puerto Rico el 6 de abril de 1906. Hizo sus estudios primarios y secundarios en las escuelas públicas de Maunabo y Humacao. Cursó sus estudios universitarios en el Harvard College donde obtuvo su bachillerato en Ciencias en el 1925; los de medicina en la Facultad de Medicina de la Universidad de Harvard de donde se graduó en el 1929. Hizo su internado en el Hospital Presbiteriano de San Juan del 1930 al 1931 y residencias en el mismo hospital del 1931 al 1935. Durante esos primeros años varió su atención entre la Medicina Interna y la Pediatría. Amplió su experiencia y cursó estudios post-graduados en diversos centros europeos del 1929 al 1930, y luego repetidas veces en el Hospital de Niños en Boston. Estuvo activo en la práctica privada de la Pediatría del 1936 al 1962 pero fue regulando y limitando su cliente-

la privada hasta tener que renunciar a ella según crecían las exigencias de los deberes hospitalarios y docentes. En el 1941 aprobó los exámenes del "Board" de Pediatría. Se unió a la facultad de la Escuela de Medicina desde el comienzo de la misma en el 1951 y fue profesor titular de Pediatría desde el 1951 hasta 1974. Fue director de los servicios de pediatría del Hospital de la Capital del 1945 al 1960 y del Hospital Distrito Universitario del 1960 al 1974. Es miembro de prestigiosas asociaciones tales como la Academia Americana de Pediatría, el "American College of Physicians," "American Pediatric Society", "Alpha Omega Alpha" y "Phi Beta Kappa".

Ha sido autor de numerosas publicaciones. Antes del 1[illegible], escribió sobre los temas de diarrea aguda en los lactantes, edema por desnutrición, drepanocitosis, laringotraqueo-bronquitis aguda, anemia hemolítica de los recién nacidos y meningitis meningocócica en Puerto Rico. Desde el 1954 ha sido autor o colaborador de publicaciones en nuestro Boletín y en revistas tales como: The "American Journal of Clinical Pathology", "Blood", "JAMA", "Journal of Pediatrics", "Pediatrics" y "Journal of Clinical Investigation". Su principal interés durante esta época ha sido en la nutrición y los problemas digestivos del lactante. Sobre este tema ha escrito capítulos para varias ediciones, incluyendo la más reciente en imprenta, del texto "Pediatrics in the Tropics and Subtropics" de Jellife. Otro de sus trabajos sobre diarrea infantil aparecerá en la edición especial sobre pediatría tropical de la revista "Archives of Child Health".

Con la ayuda de su ejemplar esposa Doña Teotista el Dr. Ortiz formó un hogar revelador de sus éxitos como esposo, padre y pediatra. Los resultados más evidentes son las cualidades personales, los logros profesionales y culturales de sus excepcionales hijas: Carmen, de la facultad médica del Columbia Presbyterian Medical Center; Dorita, Trabajadora Social del Hospital de Veteranos de San Juan; Idalia, Arquitecta; y Gloria, Catedrática de Inglés de la Universidad de Puerto Rico.

En el 1974, concluyó su tarea como Director del Departamento, pero ha seguido en la cátedra, dando el ejemplo del maestro modelo; académico puro y pediatra general completo.

Es con profundo respeto, cariño y gratitud que la Facultad del Departamento de Pediatría ofrece esta edición del Boletín de la Asociación Médica de Puerto Rico en honor a quien honor merece.



Antonio Ortiz, M. D.

Director Departamento de Pediatría (1952 - 1974)
de la Escuela de Medicina de la
Universidad de Puerto Rico

MORTALIDAD INFANTIL EN NUESTRO MEDIO

Antonio Ortiz, MD, FAAP, FACP, APS

Le hemos pedido al Dr. Antonio Ortiz que escriba los primeros artículos de esta edición del Boletín. Ha sido nuestro deseo que estos artículos del Dr. Ortiz sean los primeros dos de la serie de publicaciones provenientes de nuestro nuevo Hospital Universitario de Niños. Los mismos reflejan su filosofía y los cambios favorables trascendentales que han sucedido en el transcurso de las recientes décadas. De éstos él ha sido protagonista y agente propiciador.

Este artículo se basa en una conferencia dictada en Santo Domingo a raíz del Congreso de Pediatría celebrado en agosto del 1974. Fue publicado en los Archivos Dominicanos de Pediatría de septiembre-diciembre del 1975 y con el permiso de sus editores, se presenta aquí, ampliado, revisado y puesto al día, para su mayor difusión entre los médicos, trabajadores de la salud, y el pueblo puertorriqueño - a quien más directamente le atañe.

La mortalidad infantil está considerada como *el mejor índice de la salud de un pueblo.* Envuelve el efecto de las condiciones económicas, sociales y culturales, y la eficiencia de los servicios médicos curativos y preventivos, individuales o generales. Es un verdadero indicador del grado de desarrollo de una comunidad en su totalidad, y podríamos decir, un espejo de su civilización.

Las cifras presentadas en la Tabla I reflejan la influencia de los factores que hemos mencionado según operan en diversos países. Fueron tomadas de los informes demográficos de las Naciones Unidas y están sujetas a ligeras variaciones que sería prolijo enumerar.

En la gráfica I se ilustra cómo declinó la mortalidad infantil en Puerto Rico en las décadas del 30 al 60. Como en todos los países en desarrollo, la llamada mortalidad tardía (infantes de 1 a 11 meses) es la que ha descendido más rápidamente, al ritmo del progreso. El cambio más significativo puede atribuírsele a la gran disminución del número de muertes por diarreas infantiles (gráfica 2).

Es característico que la mortalidad neonatal, el otro gran bloque de las defunciones infantiles, ha descendido más lentamente (gráfica I). En consecuencia, constituye una fracción relativamente más y más elevada del total de defunciones según el progreso va eliminando las causas de muertes tardías. Los diversos factores que la determinan no son tan fáciles de eliminar, aunque es

Del Departamento de Pediatría, Escuela de Medicina, Recinto Universitario de Ciencias Médicas, Universidad de Puerto Rico, San Juan, Puerto Rico 00936. Publicación Núm. 1 del Hospital Universitario de Niños.

TABLA I
MORTALIDAD INFANTIL
1973
(Por mil nacidos vivos)

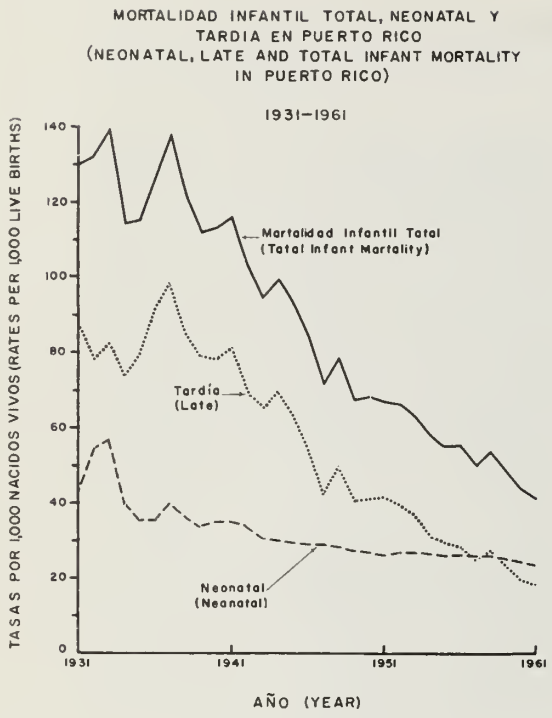
Canada	17.6	Alemania Occidental	23.2
Estados Unidos	18.5	Dinamarca	14.2
Puerto Rico	24.2 (20.9 en el 1975)	Reino Unido	18
Cuba	36	Francia	13.3
Jamaica	39	Suecia	11.1
Guadalupe	45	Noruega	12.7
Barbados	42	Unión Soviética	22.6
República Dominicana	64	Japón	13
El Salvador	53	Turquía	119
España	27.9	Australia	17.3
Guatemala	88	Egipto	118
Ecuador	91	Israel	23
Colombia	76	Irak	104
Venezuela	49	India	139
Surinam	30	Hong Kong	19
Argentina	58	Congo	180
Chile	88	Guinea	216
Mexico	69	Pakistán	142
Uruguay	43	Filipinas	67

verdad que el bajo peso al nacer y la incidencia de la prematurez responden gradualmente a la mejoría en los niveles de vida y más directamente al buen cuidado y la adecuada alimentación de las madres embarazadas. Mucho ha contribuído el refinamiento en la atención médica y de enfermería brindados a los recién nacidos. Los prematuros y los bebés de alto riesgo se han beneficiado enormemente con las unidades de cuidado intensivo desarrolladas en diversos centros.

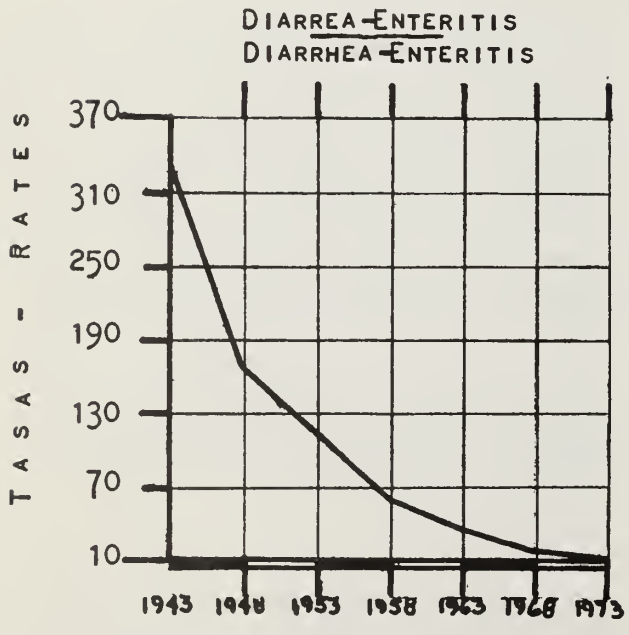
Es un dato significativo que la mortalidad entre los niños de 1 a 4 años es aún proporcionalmente más alta en los países pobres (Tabla II). El estado de salud de este grupo refleja mejor la situación ambiental y es un índice aún más sensitivo del desarrollo social-económico de una comunidad y de la efectividad de sus servicios médicos y sanitarios. No se le ha prestado mucha atención a este fenómeno porque la mortalidad entre los pre-escolares no envuelve un número tan elevado de víctimas, olvidando que la elevada morbilidad en este grupo siempre deja sus huellas.

Los llamados pre-escolares ya no gozan de los íntimos cuidados maternos, sobre todo efectivos si incluyen la alimentación al pecho, y de la estrecha vigilancia y protección que le brinda la familia al lactante. Los niños mayorcitos, tantas veces olvidados, pasan a ser verdaderas criaturas de la comunidad, y en un grado superlativo, su responsabilidad. La tendencia es a olvidar y descuidar el intenso ritmo de desarrollo psíquico y motor del pre-escolar y su significado en la formación del hombre del mañana, en nuestra legítima preocupación por la pavorosa mortalidad entre los lactantes. Debemos reconocer que mientras más tierno el infante, tanto más sensitivo y vulnerable al ambiente. En ellos debemos concentrar nuestros recursos, amplios o escasos. Esto no exige ni justifica el que abandonemos a los pre-escolares. Lo decisivo es el énfasis en las primeras etapas de la vida.

Más allá de la mortalidad está envuelta la morbilidad, el desarrollo integral, el bienestar y la felicidad de los niños, que constituyen el factor determinante de la calidad de la vida de los individuos y la sociedad del futuro. El porvenir de todos los países lo forjan



Gráfica 1



Gráfica 2

sus niños. La elevada mortalidad en la infancia y la niñez implican mayor número de niños enfermizos, desnutridos y defectuosos que no gozarán de pleno vigor como adultos. Recordemos el viejo proverbio castellano: "árbol que crece torcido nunca su tronco endereza", y la más antigua y profunda exhortación de Sócrates a los ciudadanos de Atenas: "Os afanáis escarbando la tierra en busca de riquezas y descuidáis a vuestros hijos, a quienes algún día habréis de dejárselo todo."

La mortalidad excesiva entre los niños de la América Latina y de otros países en desarrollo es motivo de preocupación genuina y legítima. Para aliviarla hay que aplicar muy eficazmente las medidas preventivas en una forma abarcadora, porque son amplias las causas y profundas las raíces del mal. El estar conscientes de los factores múltiples envueltos, del encadenamiento y la interacción de diversas causas nos ayudará enormemente a enfrentar el problema. Por ejemplo, es de todos sabido que las diarreas infantiles son la causa principal de muerte después del período neonatal. La mayoría son desencadenadas por un proceso infeccioso, pero detrás de la infección está la desnutrición que hace más susceptible y frágil al bebé, el bajo peso al nacer, la prematurez, la suciedad del ambiente y la contaminación de los alimentos, la ignorancia de los familiares y una concatenación de circunstancias. Obviamente el enfoque tiene que ser multifacético.

Casi nunca es la causa inmediata o aparente lo que explica lo que está sucediendo — hay que ir más allá a los mecanismos básicos y fundamentales que son de índole socioeconómicos y cultural. Las tristes consecuencias son efectos de la pobreza y la desigual distribución de la riqueza, de la ignorancia, y de la defectuosa organización social. Estos son los grandes enemigos que tenemos que v encer. Trabajan en *reciprocidad perversa* para promover el hacinamiento, falta de limpieza y contaminación del ambiente, servicios médicos y sociales inefectivos y sobre todo, la desnutrición que se combina con las infecciones para diezmar a nuestros niños.

En Latino-América la desnutrición de las grandes masas poblacionales juega un papel fundamental. Según el estudio de Puffer y Serrano, la mala nutrición es causa básica o asociada en el 35 por ciento de las muertes infantiles — en el 52 por ciento si se excluyen las muertes neonatales. La carencia en la madre embarazada es un factor importante en la prematurez y el bajo peso del bebé al nacer, que multiplican los riesgos. La mala alimentación del bebé detiene o retrasa

TABLA II
MORTALIDAD MATERNA, INFANTIL Y EN LA NIÑEZ EN LA GRAN BRETAÑA COMPARADA CON LA DE ALGUNOS OTROS PAISES. (TOMADA DE C. WILLIAMS)

País	Mortalidad por 1,000 habitantes	Natalidad por 1,000 habitantes	Mortalidad materna por 1,000 nacimientos	Mortalidad infantil por 1,000 nacidos vivos	Mortalidad por 1,000 de la misma edad - 1 -4 años, 5-9 años	
Gran Bretaña-1962	9	16	0.4	21	0.8	0.5
Jamaica -1950	13	31	6	86	13	1.0
Egipto - 1947	22	38	20	205	49	4.3
Puerto Rico - 1960	6.7	32		43.7	3.1	
1967				31.9	1.2	
Estados Unidos de América - 1966				23.1	1	

su desarrollo y pone en peligro su supervivencia y bienestar. Los estragos de las infecciones, tales como la gastroenteritis, sarampión y otras, en los niños desnutridos o mal desarrollados, están plenamente demostrados.

La deficiencia fundamental es en proteínas, sobre todo en proteínas de origen animal. En situaciones de hambre colectiva son los niños los que más sufren, en parte por su débil posición competitiva y su dependencia, en parte porque debido a su rápido crecimiento y desarrollo sus necesidades nutricionales son más intensas y perentorias y exigen alimentos de superior calidad biológica (en la práctica proteínas de composición variada, preferiblemente de origen animal, que son más escasas y costosas). Debemos estar conscientes que los efectos de la privación son especialmente deletéreos desde antes del nacimiento y sobre todo en las primeras semanas y meses de vida del bebé, cuando están en juego su resistencia a las infecciones y su desarrollo total, su supervivencia y su porvenir. Peligran sobre todo en el infante y el pre-escolar el desarrollo del cerebro y por supuesto la inteligencia en una época de acelerado crecimiento y refinamiento del sistema nervioso central.

Hay muchos familiares que se acostumbran al subdesarrollo de los niños porque no tienen con quien compararlos que no sean otros niños y adultos igualmente desnutridos. La carencia larvada c insensible engaña a comunidades enteras y aún a los propios médicos. A pesar de ello se podrían detectar en los niños mayorcitos cambios que a menudo pasan desapercibidos en el bebé. Lo triste es que mientras más tierno el infante más disimulada es la carencia y más profundos sus efectos sobre la composición y la función del cuerpo. A menudo las deficiencias ni se descubren ni se corrigen a tiempo.

Como hemos dicho antes, la alimentación es un factor determinante en la salud del niño, su morbilidad y su mortalidad, su grado de desarrollo. Desgraciadamente hoy en día las dos terceras partes de la población del mundo sufre de algún grado de deficiencia alimentaria. La desnutrición colectiva es el problema número uno de la salud mundial.

Afortunadamente en algunas regiones la alimentación al pecho todavía conserva la vida de millones de bebés — su papel tradicional e histórico. Pero hoy en día se utiliza poco la alimentación natural. Donde más se emplea es en los países pobres de Africa, Asia y América, pero muchas veces en circunstancias que sólo demoran el desarrollo de la desnutrición a las temidas diarreas infantiles.

La contaminación de los alimentos siempre ha sido un peligro notorio. Nos recuerda que siempre debemos preconizar la alimentación al pecho como el mejor seguro de vida para el bebé. Hoy en día con la pasteurización de la leche, la refrigeración, la variedad de alimentos disponibles y el cuidado en su manejo, y la disponibilidad de agua limpia en abundancia, se han hecho grandes progresos. Pero este régimen protector es solo posible en un ambiente ya favorecido.

En Puerto Rico hemos tenido la suerte de que en medio del rápido desarrollo económico y cultural los

servicios sociales y la ayuda al pobre se han concentrado en la provisión y distribución de alimentos. Sin menospreciar otros factores, ésto ha traído por consecuencia un gran progreso en todos los índices de salud.

En mi opinión, aunque a veces en forma insensible, los mayores beneficios han surgido de una notable mejoría en la alimentación del pueblo. Las perspectivas son magníficas porque en nuestro país los programas de asistencia social a través de la alimentación son cada día más intensos y abarcadores. Estos programas son atendidos en parte por nuestro propio desarrollo económico pero mayormente por fondos federales asignados a la asistencia social. Entre ellos hay que mencionar el seguro social, la ayuda económica directa a los necesitados, los comedores escolares y los cupones de alimento. Estos últimos, al asegurarles una alimentación adecuada a las familias pobres que constituyen más de la mitad de las familias puertorriqueñas, transformarán el cuadro de la salud en Puerto Rico. Sus beneficios se dejarán sentir lenta pero contínuamente y serán incalculables.

Mucho más prominente y fácil de comprender es la relación de la mortalidad infantil con el desarrollo económico. Sin embargo, la relación no es necesariamente lineal ni es directa. Los Estados Unidos, el país más rico del mundo, tiene una mortalidad más alta (17.3) que una docena de otros países más pobres, entre los que se destaca Suecia con una mortalidad de 11.1 por mil. Median factores como la distribución de la riqueza, los programas de salud y asistencia, y la organización social. Como yo le digo a mis estudiantes: En Suecia todos son suecos – allí hay menos desigualdades y los servicios sociales y de salud son muy extensos y cubren toda la población.

Los países árabes productores de petróleo muestran una elevada mortalidad infantil en medio de su opulencia.

Mucho depende, como dije antes, de la distribución de la riqueza, de la utilización de los recursos, de la educación, de los programas sociales, los servicios de salud, los problemas poblacionales, y otros factores. Envuelto en todo ello hay un elemento ineludible de justicia social.

Los recursos económicos, sabiamente utilizados, promueven todo el nivel de vida (que incluye viviendas, alimentación, limpieza del ambiente) la educación y los demás servicios a los que tiene derecho el hombre. No actúan por sí solos y pueden desviarse o emplearse mal. Lo que tenemos que recordar siempre es que *los recursos que se emplean en educación y salud no son gastos sino inversiones.*

También quiero recalcar el papel de la educación en la salud de los pueblos. Son muy conocidas las estadísticas de que la mortalidad infantil en las familias desciende según se eleva el nivel de escolaridad de los padres. Sin duda, la educación tampoco actúa aisladamente porque la acompañan ingresos más elevados, un nivel de vida y un ambiente más propicio y otras ventajas. De todas las medidas sociales la educación es la que se puede distribuir con mayor equidad y eficiencia. No exige enormes recursos ni insuperables sacrificios para hacerla asequible a los más necesitados. Es una bendición para todos *y más que nada la única esperanza del pobre.*

Si la ignorancia es "la peor de las tinieblas", como decía Shakespeare, imagínense cómo actuaría acompañada de la miseria.

La educación a que me refiero, la que verdaderamente gobierna el destino de los pueblos y la salud y bienestar de sus ciudadanos es la que desarrolla la capacidad intelectual de un pueblo y un sano sentido de los verdaderos valores morales y espirituales. No se limita a la capacitación técnica o vocacional a ser aplicada directamente a los problemas económicos o de salud individuales o colectivos. Tampoco se limita a grupos ni a materias específicas sino que envuelve la preparación general de toda la comunidad. Es útil el entrenamiento específico, es importante que haya expertos en ingeniería, leyes y economía, y médicos y personal adiestrado en todos los campos de la salud y la labor sanitaria, pero aún más importante es que se formen líderes y que se plasme una comunidad educada e inteligente en un amplio sentido. Esa comunidad sabría responder a la orientación que se le brinde y multiplicaría sus esfuerzos y su rendimiento *ayudándose a sí misma.*

Podríamos utilizar como ejemplo a Puerto Rico, donde ha aumentado el número de niños matriculados en las escuelas públicas de 220,000 a 800,000 en cuarenta años (Tabla III). En ese mismo tiempo la Universidad de Puerto Rico ha crecido de 5,000 a 55,000 alumnos. Igual fenómeno se ha observado en la matrícula de las escuelas primarias, secundarias, y universitarias privadas. Además de expandir la matrícula, hemos luchado por la excelencia.

En el campo de la salud el mayor impacto ha provenido de la Escuela de Medicina iniciada en el 1950, la Escuela de Salud Pública, y la Escuela de Odontología. En el Recinto de Ciencias Médicas se entrenan más de mil personas como auxiliares en todos los campos de la salud (enfermeras, técnicos de laboratorio, dietistas, edu-

TABLA III

Puerto Rico	1930-40	1970-71
Producto nacional total	278 millones	5,168 millones
Total niños en escuelas públicas	297,468	821,046
Total matrícula U.P.R. y otros colegios	5-6,000	55,000 - 73,170
Analfabetismo	31.5 °/o	10.8 °/o
Per capita $121 (1939)	$493 (1960)	$1,600 (1972)
Familias bajo nivel de pobreza	59.6 °/o (1974, Criterios federales)	

cadores en salud, higienistas y técnicos dentales, etc.)

Los pediatras, y nuestros compañeros en el campo de la salud, estamos orgullosos de nuestra labor médica, y más orgullosos de nuestra contribución como orientadores y agentes catalíticos. Hay que hacer notar que el número de pediatras aumentó vertiginosamente en Puerto Rico en los últimos cuarenta años. Desde el 1940 contamos con residencias reconocidas internacionalmente en Pediatría y poco después en otras especialidades médicas.

Han ocurrido notables progresos en la vivienda, en el abastecimiento de agua y en la limpieza del ambiente. Los servicios de medicina preventiva se han extendido notablemente y hoy en día trabajan eficientemente en un Programa Regional con sus Centros de Salud locales respaldados por hospitales que rinden servicios a los niveles primarios, secundarios y terciarios. Se estimula la medicina de familia y la participación de la comunidad para reforzar la función social de la medicina. En lo que se refiere a la salud infantil ha sido muy útil un programa magnífico de Cuidado Materno-Infantil.

Los servicios clínicos también ha mejorado y probablemente se amplíen aún más si se planifica y se implementa adecuadamente el programa de Seguro de Salud Integral que se contempla.

Ahora mismo está funcionando el nuevo Hospital Universitario de Niños acabado de construir, con capacidad de 300 camas, con todas las facilidades modernas, entre ellas laboratorios especializados, amplias salas de juego, unidades de cuidado intensivo generales y específicamente para recién nacidos (prematuros y bebés de alto riesgo). Más que un centro hospitalario y de consulta externa, constituye la soñada casa del niño para la atención global del niño sano, enfermo, o defectuoso. Incluye las facilidades para Niños Lisiados, una unidad adscrita de Cuidado Materno Infantil y otras agencias en contacto con la comunidad.

Afortunadamente, cuando han surgido nuevos programas de servicios sociales y de salud, hemos contado con el personal entrenado para llevarlos a cabo con dedicación y eficiencia.

En Puerto Rico han ocurrido paralelamente grandes progresos en el desarrollo económico, en la educación, en la asistencia social (sobre todo en la alimentación), y en los servicios de salud que en gran parte explican el descenso de la mortalidad infantil de 139.4 a 24.2 (20.9 en el 1975) y de las muertes por diarreas infantiles de 8,000 a 156 en cuarenta años. (69 en el primer año de vida) -- (Tasa de 5 por 100,000 habitantes).

Hoy en día podemos decir, sin vanagloria o condescendencia, que nuestra tasa de mortalidad infantil es la más baja en Latino-América. Lo decimos con el único propósito de que nuestra experiencia pueda servir de guía y de estímulo a los países hermanos. Después de todo, las causas de la excesiva mortalidad infantil son prevenibles, como lo ilustran los progresos realizados en los países en desarrollo. Hay esperanzas para todos.

Creo haber esbozado los factores determinantes

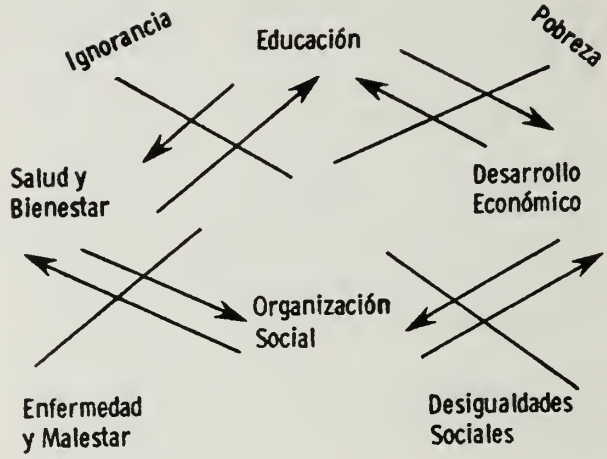
de la mortalidad infantil. Estos se resumen en la gráfica 2. Podríamos mencionar otros que de hecho son secundarios a los ya mencionados: higiene ambiental y personal, los servicios médicos y sanitarios, abastos de agua, lugar de residencia (urbana o rural), vivienda, número y orden de nacimientos, etc. Ya hemos hablado de la importancia de la salud y alimentación de la madre. Sin duda el *exceso de población hace más complicado el problema en todas sus fases* y crea una situación como el suplicio de Sísifo, en el que todos los esfuerzos se frustran ante la continuada explosión poblacional.

Pueden eliminarse el clima y la raza como elementos decisivos en la mortalidad entre los niños. Hace unos años la situación era tan grave en los climas templados y fríos como lo es hoy en los países subdesarrollados del trópico. Todavía existen zonas de desastre en países prósperos en climas fríos. Tampoco podemos echarle la culpa o darle crédito a los distintos sistemas y regímenes políticos cuya acción es secundaria. La responsabilidad no es de grupos o personas en particular, sino de la comunidad entera.

La calidad y la distribución de los servicios médicos y sanitarios son muy importantes, pero la paradoja es que donde más se necesitan es donde peores son. La *verdadera enfermedad es el subdesarrollo*, y tenemos que vencerlo con la industrialización y el desarrollo económico, una educación de calidad, y medidas sociales bien orientadas y justicieras. Solo así podremos darle marcha atrás al círculo vicioso que nos abruma.

Las medidas preventivas efectivas son generales y son más bien de índole socioeconómica y cultural - manifestaciones del progreso. El médico debe contribuir en la tarea atendiendo a la comunidad *en forma integral* en todo lo que atañe a su salud y bienestar. *Donde los recursos son escasos deben concentrarse en las etapas tempranas de la vida.* La salud y la alimentación de las madres embarazadas, del bebé recién nacido o en los primeros meses de vida deben recibir atención preferente.

Mientras resolvemos los problemas fundamentales



FACTORES DETERMINANTES DE LA MORTALIDAD INFANTIL

Gráfica 3

debemos continuar luchando por mejorar la calidad de la vida de nuestros niños. No basta con que el niño sobreviva: hay que procurarle desde antes de nacer la mejor oportunidad para el desarrollo óptimo y el disfrute máximo de su potencial físico, mental y emocional. Una buena educación debe estar al alcance de todos. Hay que atender temprano los pequeños defectos e incapacidades y los problemas psicológicos. La alimentación debe ser óptima y no apenas suficiente para evitar carencias. No basta con que el ambiente físico y social en que convive no le sea dañino - debe serle favorable en un sentido positivo. *Un niño no es verdaderamente saludable si no es un niño feliz, y para ello hay que brindarle más que nada cariño, comprensión y calor humano.*

BREVE RESEÑA HISTORICA SOBRE EL DESARROLLO DE LA PEDIATRIA EN PUERTO RICO

Antonio Ortiz, MD, FAAP, FACP, APS

En el lento progreso de las civilizaciones llama la atención lo tardío del reconocimiento del valor particular de la vida y el bienestar de los niños en el porvenir de esas mismas civilizaciones. Aunque se mencionan los niños en los códigos de Babilonia, y en los papiros de Egipto, y en Grecia, en Roma, y en la Europa medieval, muy poco se hizo hasta fines del siglo XVIII para protegerlos categórica y efectivamente, y para propulsar el desarrollo de su potencial. Se dependía de los cuidados maternales y familiares, de los asilos para niños abandonados o desamparados, y uno que otro de esos gestos de caridad que a menudo resultan efímeros e inconstantes.

Se establecieron dispensarios y hospitales separados para niños enfermos a fines del siglo XVIII en Inglaterra y poco después en otros países de Europa y finalmente en América.

Durante el siglo XIX gradualmente se destacó la Pediatría como una especialidad aparte aunque no fue hasta fines del siglo que se estableció con bases sólidas y se reconoció la posición especial de los niños. El gran progreso social impulsado por los ideales de la revolución francesa y las exigencias del desarrollo industrial se había extendido paulatinamente a las mujeres y a los niños.

No fue hasta fines del siglo XIX que las escuelas de medicina y los tribunales examinadores reconocieron que la medicina de los niños era tan genuinamente particular e impoetante que merecía considerarse como una disciplina aparte.

Hoy en día en Rusia hay diversos tipos de Escuelas de Medicina y algunas están diseñadas para enseñar medicina de niños desde el principio hasta el fin de la carrera – un enfoque que reconoce que los niños no son pequeños adultos y que son tan valiosos a la sociedad que se merecen que se les brinde una atención especial.

Del Departamento de Pediatría, Escuela de Medicina, Recinto Universitario de Ciencias Médicas, Universidad de Puerto Rico, San Juan, Puerto Rico 00936. Publicación Núm. 2 del Hospital Universitario de Niños.

Como se ve la Pediatría es una especialidad muy joven. En Puerto Rico su desarrollo ha sido más lento todavía, a pesar de que como es característico de los países en desarrollo, la proporción de habitantes en la edad pediátrica es elevada y muy alta la morbilidad y la mortalidad entre ellos.

En vista del fondo histórico, no es extraño que en Puerto Rico, isla al fin y con poco albedrío, no se conocieron bien los problemas especiales de salud del niño a principios del presente siglo. La historia del desarrollo ocurrido en Europa y Norteamérica inevitablemente se repitió, pero llegó a nosotros con un ritmo más lento y con retraso. Había unos pocos especialistas en otros campos de la medicina, y a menudo a los niños los atendían someramente los generalistas que tenían otros diversos problemas que atender. Algunos de ellos le daban preferencia a los menores y se superaban brindándoles sus cuidados con tesón y cariño. Salud Pública tenía graves problemas generales que atender y se enfrascó en ellos. Se dejó notar cierta indiferencia en los organismos oficiales hacia el bienestar y la salud del niño.

Pero la especialización se imponía frente a situaciones tan graves y complejas. Pronto habría cirujanos, como ocupación aparte y uno que otro especialista en diversas ramas de la medicina, pero no había continuidad en la formación y entrenamiento del personal especializado.

En el 1937 fue reconocido por la Asociación Médica Americana el internado general ofrecido por el Hospital Presbiteriano – el primero en ser acreditado. En el 1941 la Junta Examinadora (Board) de Pediatría certificó el entrenamiento de residentes en el servicio de Pediatría de ese hospital (que solo contaba con 14 camas para niños) como un año de entrenamiento acreditado en la especialidad. El reconocimiento se hizo extensivo al servicio de Pediatría del Hospital de la Capital, bajo la misma dirección, en el 1945. En el 1948 el Joint Council de la AMA ya estaba en acción y acreditó el servicio de Pediatría del Hospital Regional de Bayamón y en el 1950 el del Hospital de la Capital (ya previamen-

te reconocido por el Board y entrenando residentes). Las Residencias principales en otras especialidades del Hospital de la Capital también fueron reconocidas en esa época.

En el 1945 se dio un paso trascendental en el desarrollo de las disciplinas clínicas y los hospitales de Puerto Rico. Un grupo de médicos encabezados por el Dr. Juan A. Pons reformó el Hospital Municipal de San Juan y elevó sus normas hasta convertirlo en un excelente taller de enseñanza clínica al fundarse nuestra Escuela de Medicina en el 1950. La creación de este modelo de atención hospitalaria en el sector gubernamental tuvo un impacto significativo en todo Puerto Rico al nivel municipal y regional y en el sector privado.

Al mejorarse los hospitales y al enfatizarse el entrenamiento de internos, residentes y demás personal se creó la tradición y el mecanismo que más tarde dio tan valiosos frutos en la pediatría y en las otras especialidades médicas. En lo que respecta a la atención de los niños se difundieron los conocimientos sobre crecimiento y desarrollo que son fundamentales para entender a los niños y cuidarlos inteligentemente. Los médicos en sus respectivas prácticas se fueron familiarizando con ciertos trastornos y enfermedades que son peculiares a la niñez tales como: los problemas especiales de los recién nacidos, sobre todo los prematuros; ciertos defectos congénitos que se manifiestan temprano; ciertas condiciones típicas del lactante y el niño pequeño como la roseola infantum, la estenosis pilórica, la laringotraqueo bronquitis, las meningitis purulentas causadas por el Hemophilus Influenza, los accidentes y los envenenamientos típicos, la naturaleza y el tratamiento de las diarreas infantiles, los estragos de la tuberculosis en el bebé y el niño, etc. La comunidad se educó paralelamente y protegió mejor a sus niños, se fue acostumbrando al seguimiento periódico y sistemático del bebé sano, lo cual incluía consejos sobre la alimentación, orientación psicológica y las inmunizaciones que eliminaron la mayor parte de las enfermedades infecciosas comunes en los niños.

En toda esta tarea colaboraron los organismos gubernamentales manteniendo al ambiente relativamente limpio y libre de contaminación. Se mejoró el abastecimiento de agua, la vivienda, y la provisión y distribución de los alimentos. Se eliminó la malaria que había sido un azote en Puerto Rico. Se controló con diversas medidas la tuberculosis. Las defunciones anuales por diarreas y enteritis del infante bajaron de más de 5,000 a menos de 100 en cuarenta años — la mortalidad infantil de 140 a 20.9 por mil nacidos vivos. Estos logros fueron el resultado del esfuerzo común y del prodigioso desarrollo socio-económico de la Isla. Sería prolijo enumerar la contribución de diversos grupos, personas, y agencias del gobierno y la comunidad y los programas como el de Niños Lisiados y los de Cuidado Materno Infantil y otros al progreso de la Pediatría en Puerto Rico.

Hoy en día contamos con magníficos centros de entrenamiento pediátrico en la capital y en la Isla. Como culminación podríamos mencionar el nuevo Hospital Universitario de Niños ubicado en el Centro Médico que acaba de abrir sus puertas, y en el que se centralizan amplias facilidades modernas para la atención integral del niño.

Poco a poco, aunque algunos dicen que vertiginosamente, se han entrenado más y más pediatras aquí o total o parcialmente fuera de Puerto Rico. La Sección de Pediatría de nuestra Asociación Médica cuenta con 280 miembros.

Se ha mantenido un intercambio saludable con centros pediátricos en los Estados Unidos y otros países, para entrenamiento general o super-especializado. Ya hay muchos pediatras especializados en neonatología, cardiología, neumología, endocrinología, neurología, nefrología, etc. Otros se han distinguido en labores administrativas, en la investigación o en la docencia, y en Salud Pública. Es significativo y altamente provechoso que ya tenemos cirujanos, psiquiatras, oftalmólogos, dentistas y muchos otros especialistas o generalistas con entrenamiento y enfoques pediátricos. Alguien ha dicho que a todos los médicos se les ha dado un toque pediátrico.

Muy importante ha sido la formación de enfermeras y otro personal paramédico bien motivado y entrenado para atender a los recién nacidos y prematuros, lactantes y niños mayorcitos con admirable destreza y dedicación. Prolijo sería enumerar a los dietistas, trabajadoras socialcs, ayudantes dentales, educadoras de salud, etc., que han reafirmado su interés y sus conocimientos en la atención de los niños.

Lo que fue una humilde semilla se convirtió en un árbol frondoso. El terreno era fértil y lo cultivaron hombres y mujeres con amor a los niños, dispuestos a luchar tesoneramente y a sacrificar sus intereses materiales para servir mejor a la sociedad en que convivimos. Con una causa tan noble siempre contamos con el respaldo y la simpatía de la comunidad, porque no hay corazón tan duro que no responda al sufrir de un niño. Hubo recalcitrantes en la buro-

cracia que hablaron del "disparate" de un hospital exclusivamente para niños y protestaron de que se invirtieran dinero y esfuerzos en salvar prematuros en medio de la crisis poblacional. Pero esos prejuicios no estaban arraigados y pronto se echaron a un lado — lo que estaba envuelto era no solo la salud del niño sino la salud del hombre del mañana. Primero se mejoró la atención médica de las necesidades inmediatas de los niños enfermos. Luego se crearon servicios completos de Pediatría dentro de hospitales generales y luego centros autónomos.

Lo importante es que desde el principio se enfatizó el entrenamiento del personal médico y el equipo de salud que iba a imprimirle continuidad y nuevos bríos a la tarea. Nuestros médicos pioneros no olvidaron que el vocablo doctor se deriva del latín "docere" que quiere decir enseñar — en el caso de los médicos no solo a sus colegas y colaboradores sino también a los pacientes y sus familiares y al público en general. No les arredró en su labor docente el espectro de la competencia futura. Firmemente se aplicó la frase de Harvey Cushing de que "es un maestro mediocre aquel a quien sus discípulos no le superan."

El establecimiento y difusión de los internados y residencias reconocidas y el entrenamiento de subespecialistas fue una de las bases fructíferas de lo logrado. Hay que reconocer también la enorme contribución de la Escuela de Medicina y de todo el Recinto de Ciencias Médicas en la formación de los profesionales de la salud.

El contínuo mejoramiento de las facilidades hospitalarias culminó con la construcción del nuevo Hospital Universitario de Niños, ya antes mencionado.

Paralelamente se reforzaron las medidas sanitarias dirigidas al saneamiento del ambiente, la medicina preventiva y la rehabilitación. Se ampliaron los servicios sociales, se mejoró la distribución y accesibilidad de los alimentos. En toda esta tarea colaboraron los pediatras, ya de por sí inclinados a esta versión amplia de la medicina. Indudablemente el desarrollo socioeconómico de Puerto Rico y el progreso en la educación del pueblo impulsó e hizo posible que se llevaran a la realidad cosas que parecían sueños años atrás.

Los pediatras del futuro deben conservar sus raíces sociales porque en la comunidad es que está su verdadero campo de acción. La comunidad entera ha estado envuelta en el progreso de la Pediatría y debemos mantenernos muy cerca de los niños, las madres, la familia y la sociedad entera en que convivimos. El pediatra de ahora y del futuro, como todo médico, debe estar consciente de su función social y debe cultivar íntimamente y en todo momento su humanidad que es la esencia de la medicina.

BRONCHIAL ASTHMA IN PUERTO RICAN CHILDREN

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The incidence and characteristics of Bronchial Asthma in Puerto Rican children are not well known. From clinical experience we have always suspected that the prevalence of asthma in Puerto Rico is high and that contributing factors are abundance of molds, varied flora and a high relative humidity. Poor living conditions and the factors that go with it, such as arthropods, insects, inadequate ventilation and crowding are probable additional hazards among the indigent. We have received several letters during recent years from health authorities, social workers and physicians from mainland United States inquiring about the incidence and characteristics of Bronchial Asthma in Puerto Rico. They express concern about the frequency and severity of Bronchial Asthma among Puerto Rican children living in cities like Philadelphia and New York.

The purpose of this communication is to examine some of the available information about the prevalence and characteristics of asthma in Puerto Rican children.

Materials and Methods

Several studies and surveys have been made during recent years. (1, 2, 3, 4). Some have been part of our Pediatric Pulmonary Center activities and others have been stimulated by our didactic activities or have been made in compliance with summer fellowship work of medical students under our supervision. The data for the various surveys have been collected in different manners. We have reviewed the information available and excluded that which we have felt is not pertinent or useless because of lack of complete information or controls. Some information has been included in spite of lack of controls because it is considered that it might be useful to future investigators of this subject.

Four surveys were reviewed:

(1) The San Juan City Hospital Survey

The cases of bronchial asthma admitted to the San Juan City Hospital during the years 1971 to 1973 were reviewed. All were children under 12 years of age and represent an urban metropolitan community with many slum areas.

(2) The Head Start Survey

This survey was conducted by a medical student who was awarded a summer fellowship by the Allergy Foundation of America under the preceptorship of one of us (PM). It included preschool children of a San Juan Head Start Program.

(3) The Descriptive Study of Asthma

This was a smaller detailed survey of 52 children selected at random from our Pediatric Pulmonary Center cases. Information about general, personal, household and clinical characteristics was obtained.

(4) The Arecibo School District Study

The survey was conducted at the Arecibo School District in the north central part of Puerto Rico including rural and urban schools. It was initiated by a health educator who participated in one of our five-day Pediatric Pulmonary Courses.

Results

San Juan City Hospital Survey

Between 1971 and 1973 fourteen hundred and forty two children with bronchial Asthma were admitted to the San Juan City Hospital. These were mostly indigent urban children. In 96 percent of the cases the initial attack occurred before the age of 6 years. In 81 percent before the age of 3 years and in 66 percent before

From the Pediatric Pulmonary Center of Pediatric Pneumology Section, Department of Pediatrics, School of Medicine, Medical Sciences Campus, University of Puerto Rico, San Juan, Puerto Rico. University Children's Hospital Publication No. 3.

This study was supported by HEW, HSA, BCH, MCHS Grant No. 950 (76-205-62-01) for the Development of Pediatric Pulmonary Care Personnel.

the age of 2 years (24 months of age). The majority were boys (66 percent).

The Head Start Survey

In 1969 five hundred and forty three preschool children of the San Juan Head Start Program were studied. In 133 (24.5 percent) there were symptoms of bronchial asthma. Of these 53 percent were boys. The first attack of asthma occurred during the first year of age in 68 percent of the children. A seasonal incidence was noted: 59 percent of the attacks occurred in the winter, 16 percent in the summer and 25 percent throughout the whole year. The homes of these children were located in different areas of San Juan and in the adjacent town of Cataño; all of them in humid areas. Of 39 children who moved to another house 24 (61 percent) reported improvement of the asthma. The asthmatic attacks occurred once or twice a month in 77 (58 percent). In the others the frequency of attacks was reported to be between every two and up to every twelve months. Allergic rhinitis was reported in 11 percent of the entire group of 543 and in 25 percent of the asthmatic group.

Descriptive Study of Asthma of the Pediatric Pulmonary Center

In this study a limited number of patients was selected at random for a detailed analysis between 1970 and 1972. These patients were admitted to the Pediatric Pulmonary Center with a diagnosis of bronchial asthma. All were under 13 years of age. The observations were made in 41 to 46 of the children for whom accurate information was available. In 67 percent the first attack of asthma occurred before the age of 2 years; in 24 percent from 2 to 6 years of age and in 9 percent from 7 to 11 years. The attacks were more frequent during the night (89 percent of the cases). Mainly between 12:00 midnight and 3:00 A. M. In 79 percent they improved during the day. The height of the children was below the third percentile in 14 percent and the weight was below the third percentile in 25 percent. A family history of bronchial asthma was present in 41 percent on the paternal side and in 28 percent on the maternal side. The attacks were associated with exercise in 44 percent and with weather changes in 70 percent. The latter was attributed to rain by 63 percent. Eczema was reported in 7 percent and wheals in 12 percent. Sensitivity to soap was reported in 4.6 percent and to insect bites in 16 percent. Tonsillectomy had been performed in 16 percent. Parasites (trichuriasis), were reported in only two of 43 cases. Enuresis was reported in 28 percent. There were dogs in 32 percent of the households and cats in 13 percent. Most of the households were built of masonry (80 percent) and only 31 percent of the children had their own bedroom. The average household had 5 persons.

The roentgenologic findings in the chest revealed increased radioluscency in 13 percent, irregular distribution of air in 39 percent, flat diagphgram in 15 percent, peribronchial infiltrations in 65 percent and increased hilar markings in 43 percent. Isolated findings were cardiomegaly and consolidation.

The Arecibo School District Study

The school teachers of Arecibo were asked to report the children who had asthma. Included were all public schools of Arecibo located in urban and rural areas. The survey included 20,000 children from 6 to 15 years of age. Information was obtained from 92 percent of the schools and 1,000 cases of asthma were reported. In 531 of the 1,000 an interview was made, usually with the mother. In most instances the asthmatic attacks began before the first grade of school, and improved temporarily with medical care. In the minority of children special studies had been done to establish the etiology of the attacks. Most of the children had asthmatic attacks within 5 months before the survey. The majority were boys in spite of the fact that there were more girls than boys in the school population. Allergy to milk was reported in 11 percent of the asthmatic children.

Seventy six percent of the asthmatic school children were from 6 to 12 years of age and 16 percent from 13 to 15 years.

The initial symptoms of the asthmatic attacks appeared during the first year of age in 25 percent, from 1 to 3 years in 34 percent, from 4 to 6 years in 25 percent, from 7 to 9 years in 9.8 percent and from 10 to 12 years in 3.8 percent. Ninety percent of the children received some form of treatment for the first attack. Seven percent were treated in a hospital. Fifty five percent were treated at public facilities and 32 percent by private physicians. The response to treatment was partial in 33 percent and there was mild temporary improvement in 58 percent. Nineteen percent were not on treatment at the time of the survey.

In 36 percent of the homes there was a cigarette smoker. Almost always (in 90 percent) the person was either the father or the mother. Fifty three percent of the patients were from urban homes and 45 percent from rural homes.

Discussion

Recent pediatric textbooks describe the incidence and prevalence of bronchial asthma in children as follows:

In Nelson's Textbook of Pediatrics (1975) it is stated that asthma is one of the leading causes of chronic illness in childhood and that prior to puberty it is twice more common in boys than in girls (5). In Pediatric Diagnosis and Treatment by Kempe (1974) it is stated that asthma affects less than 10 percent of the population and that the onset of attacks is rare during the first year of life (6). In Davidson's Compleat Pediatrician (1969) the average onset of asthma is reported to be around 3 to 5 years of age and the incidence in children 24.5 per thousand (7). In Brenneman's Practice of Pediatrics (1972) a study is quoted of a community in Michigan. Asthma affected 4.1 percent to 5.1 percent of the general population; in 32 percent the onset was before the age of 4 years and in 50 percent before the age of 15 years (8).

In Immunologic Disorders in Infants and Children (1973) Pearlman states that the onset of bronchial asthma is usually within the first six years of life; often in infancy, and that it affects about 3 percent of all children (9). In Disorders of the Respiratory Tract in Children, Volume one (1972), Susan Deer reports that children under 17 years of age are affected by asthma at a rate of 25.8 per thousand (10). She quotes a 1957 survey from London in which asthma affected 6.6 to 9 percent or more of the children examined in a pediatric practice. This was at the time when the air contamination problem in London had not been solved. Among children 6 to 17 years of age the U. S. National Health Survey reported asthma in 5 percent to 7 percent of the children (4 percent at the age of 6 years, 7 percent at 7 years and 5 percent at 12 years) (1).

In Puerto Rico, the results of the surveys we have reviewed suggest that the prevalence of bronchial asthma is high. From the Arecibo survey it can be estimated that it affects around 54 per thousand school age children. * In the San Juan Head Start group the prevalence of bronchial asthma was startingly high. Twenty four percent of preschool age children had bronchial asthma. This figure is difficult to question because the history was obtained and the patients were examined by a physician. The descriptive study of our Pediatric Pulmonary Center provides information that coincides with that of the other surveys in regard to onset. In addition it suggests that bronchial asthma is not being confused with pulmonary migration of parasites as often as we thought it might be. In only two cases parasites were found and they were of the type that does not produce pulmonary symptoms (trichuriasis). Becuase this is a selected group already diagnosed we still believe that parasites mainly Ascaris lumbricoides and Toxocara cani, may play a role in the clinical manifestations of bronchial asthma among some Puerto Rican children. One factor which needs further study concerns the environment of the public schools. Many have frame ceilings which harbor bats and are corroded by termites. Allergy to termites, bat antigens or wood dust are factors which need further investigation.

Asthma in Puerto Rican children appears rather frequently in the first two years of life. The frequency of onset during the first year of life of 68 percent in the San Juan Head Start group is much higher than that reported elsewhere.

The information available from the Arecibo School District group about health care in the asthmatic children suggests that treatment is of sporadic nature and that diagnostic and preventive measures are inadequate.

Conclusions

Bronchial asthma is highly prevalent in Puerto Rican children. Usually it begins before the age of 6 years and often during the first year of age. We estimate that among the school population of Puerto Rico in 1972 (97,410 for public schools and 85,094 for private schools) about 42,255 children were affected by asthma. It appears that medical care and preventive

** - Estimated as follows: There were 20,000 children in the School District. Information was obtained for 92 percent; that is, 18,400. One thousand cases of asthma were reported among this group (1000/18,400 = 0.054).*

measures are not adequate for most of the affected children. The problem is serious and merits further research concerning its frequency, etiology, prevention and improved delivery of health care to these children.

Conclusiones

La prevalencia de asma bronquial en los niños puertorriqueños es alta. Con frecuencia aparece antes de los 6 años de edad; a menudo durante el primer año de vida. Hemos calculado que en la población escolar de Puerto Rico en el 1972 (97,410 estudiantes de escuelas públicas y 85,098 de escuelas privadas) habían 42,255 niños afectados por asma. Los servicios de atención médica y las medidas preventivas no parecen ser adecuadas para la mayoría de los niños afectados. Es un serio problema que merece investigarse más detenidamente en lo que concierne a frecuencia, etiología, prevención y mejores servicios de salud para estos niños.

Reconocimientos

El Estudio de Alumnos Que Sufren de Asma del Distrito Escolar de Arecibo, fue realizado con la participación de la Asociación Puertorriqueña del Pulmón, el Programa de Salud Escolar, Departamento de Instrucción y las siguientes personas del Distrito Escolar de Arecibo: Sra. Luisa M. Ayala de Cabrera; Srta. Angelina Cruz; Sra. Luz Minerva Martínez; Sra. Lydia A. Morell; Srta. María D. Zeno; Sra. Marixa Gómez; Sr. Israel Serrano; Srta. Aida L. Rodríguez; Sra. Jenny Natal; Sra. Gloria A. Soberal; Sra. Rosalina Alvarez; Sra. Modesta Olmo de González; Sra. Aida Capetillo de Román; Sra. Mixaida Santiago; Sra. Luz Elba Cardona; Sra. Isabel M. Soto de Ríos; Sr. Eugenio Candelaria; Sra. Flavia Ramos de Rivera; Sra. Aida I. González; Sr. Angel Gutiérrez.

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METACONDROMATOSIS: DILEMA DIAGNOSTICO. A PROPOSITO DE ESTUDIOS EN UNA FAMILIA PUERTORRIQUEÑA

Francisco de la Cruz, MD

José M. García-Castro, MD

En 1971, Maroteaux caracteriza una enfermedad ósea la cual llama metacondromatosis (1). Esta se distingue por la asociación poco usual de lesiones similares a las de dos desórdenes óseos de naturaleza diferente, la exostosis múltiple hereditaria (2) y la encondromatosis o enfermedad de Ollier (3). La peculiaridad de la localización de las lesiones, su aspecto radiológico, su evolución y su patrón hereditario hacen de la metacondromatosis una entidad aparte.

Recientemente hemos tenido la oportunidad de evaluar a una familia puertorriqueña con hallazgos clínicos, radiológicos y genéticos indicativos de la metacondromatosis. Nuestros hallazgos motivan esta comunicación, siendo ésta la cuarta familia descrita en la literatura médica con metacondromatosis y la primera en Puerto Rico.

Informe de Casos

La familia evaluada consta de tres miembros: madre y sus dos hijas, todas residentes en Guaynabo.

Caso Núm. 1:

J. C. B., hembra, nació el 1ro. de agosto de 1967, la primera hija de un matrimonio no consanguíneo, ambos de 20 años de edad al momento de la concepción. El embarazo, a término, estuvo libre de complicaciones excepto por albuminuria en el octavo mes. El parto fue por cesárea debido a desproporción cefalo-pélvica. El peso al nacer fue de 3,175 gms y la talla 55.88 cms. Su desarrollo y estado de salud fueron normales hasta los 4 años, cuando se observa una protuberancia en la muñeca izquierda, la cual al ser evaluada radiológicamente fue diagnosticada como una exostosis solitaria, sin requerimientos terapéuticos. El 4 de marzo del 1974, a la edad de 6 7/12 años, fue evaluada nuevamente al notarse la proliferación de las lesiones que ahora envolvían el dedo índice de la mano derecha, ambas muñecas, rodillas, tobillos y hombros. Se establece entonces un diagnóstico de exostosis múltiple hereditaria y se refiere a nuestro servicio. Al examinarla, encontramos que se trata de una niña de estatura normal, 127.0 cms, con deformidad de la muñeca derecha y desviación cubital del dedo índice derecho, además de protuberancias óseas bilaterales en muñecas, hombros, rodillas y tobillos, las cuales no producen dolor ni limitación de movimiento. El resto del examen físico fue normal. Conjuntamente con este paciente nos fue referida su hermana menor, cuyo caso procederemos a describir.

Caso Núm. 2:

C. C. B., hembra, nació el 28 de junio de 1968, el segundo embarazo del matrimonio antes descrito, el cual fue normal y a término. El parto fue por cesárea debido a cesárea previa. El desarrollo y crecimiento de la niña fueron normales. A la edad de 5 4/12 años, se comenzó a notar protuberancias óseas semejantes a las de su hermana, lo cual motivó una evaluación radiológica. El diagnóstico fue exostosis múltiple hereditaria. Luego fue referida a nuestro programa. Al evaluarla, encontramos que su talla es normal, 124.5 cms, como fue el resto del examen, salvo por protuberancias óseas en la parte distal de las falanges proximales 2 al 5 izquierdas, en las rodillas y los tobillos. Los hallazgos clínicos y el diagnóstico presuntivo de exostosis múltiple hereditaria nos indujeron a estudiar también a la madre de las niñas.

Caso Núm. 3:

C. B. S., hembra, nació el 31 de enero de 1945. Su estado de salud siempre ha sido normal y nunca había tenido que ser evaluada por desórdenes óseos. Su talla es de 142 cms. Al hacer nosotros estudios radiológicos, nos percatamos de la presencia de lesiones óseas.

Hallazgos radiológicos y de laboratorio

La evaluación minuciosa de los estudios radiológicos nos

Del Departamento de Pediatría, Hospital Regional de Caguas y Programa Médico Regional de Enfermedades Hereditarias y la Sección de Genética Médica, Departamento de Pediatría, Escuela de Medicina, Recinto Universitario de Ciencias Médicas, Universidad de Puerto Rico, San Juan, Puerto Rico 00936. Publicación Núm. 4 del Hospital Universitario de Niños.

Subvencionado, en parte, por el donativo 76-203-83-56, del Programa Médico Regional de los Laboratorios Nacionales de Salud, Bethesda, Maryland.

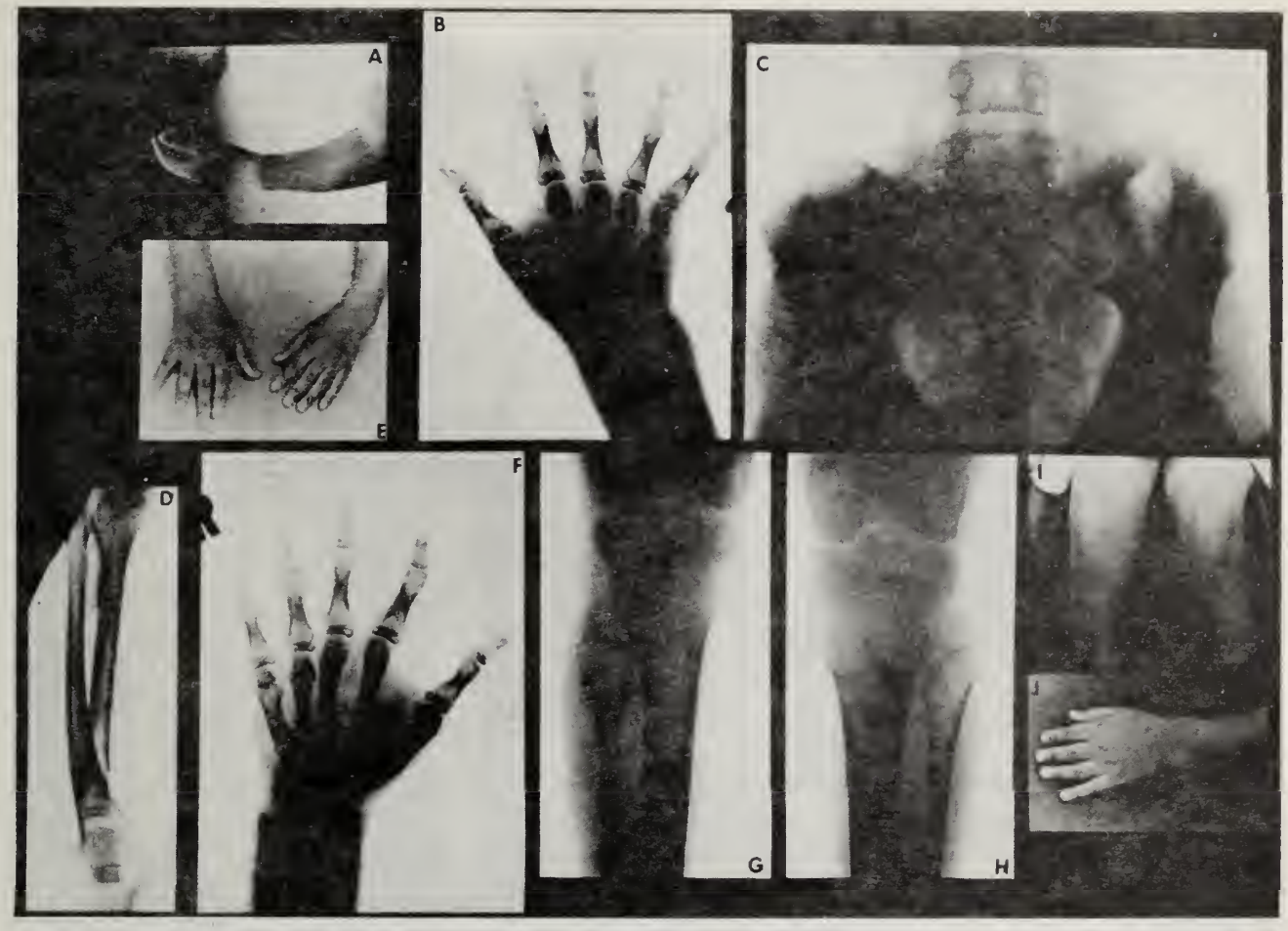


Fig. 1: *Caso 1 J.C.B. - A, E, I, J, Protuberancias óseas en dedos, muñecas y rodillas. Encondromas - B- Falange 2 derecha proximal F, I. Ambas crestas iliacas borde superior. Exostosis - D, G, H.*

demostró la presencia de dos tipos de lesiones: exostosis (lesiones metafisiarias de base ancha y ápice alejándose de la epífisis) y encondromas (lesiones localizadas usualmente en el centro de la metáfisis, cuyo ápice tiende a apuntar hacia la epífisis). Estos hallazgos; como discutiremos luego, alteran el diagnóstico hasta entonces sostenido. En la Tabla 1 presentamos la distribución de las lesiones por tipo y por caso estudiado. Otros estudios de laboratorio incluyen cariotipo, urinálisis, hemograma y SMA-12, siendo todos normales en los tres pacientes.

Discusión

La exostosis múltiple hereditaria fue descrita por primera vez por Stanley en 1849 y su patrón de herencia dominante lo demostró Stocks y Barrington en 1925 (4). Desde entonces se han publicado series extensas mostrando los hallazgos radiológicos y genéticos característicos de la enfermedad. Por otro lado, la encondromatosis o enfermedad de Ollier (3) se conoce desde 1899, no habiéndose encontrado en ella un patrón de herencia. En 1971, Maroteaux define una nueva entidad patológica ósea que denomina metacondromatosis, donde se asocian elementos de ambas entidades descritas, pero con peculiaridades propias, lo que hace de la metacondromatosis un ente aparte (1).

En la exostosis múltiple hereditaria las lesiones son metafisiarias, de base ancha y ápice alejándose de la epífisis, y se localizan característicamente en los huesos largos, con menor frecuencia en metacarpos, falanges y pelvis. En la encondromatosis, por el contrario, las lesiones, aunque también metafisiarias, tienden a tener una posición central con ápice señalando a la epífisis. Las ubicaciones preferentes son los huesos

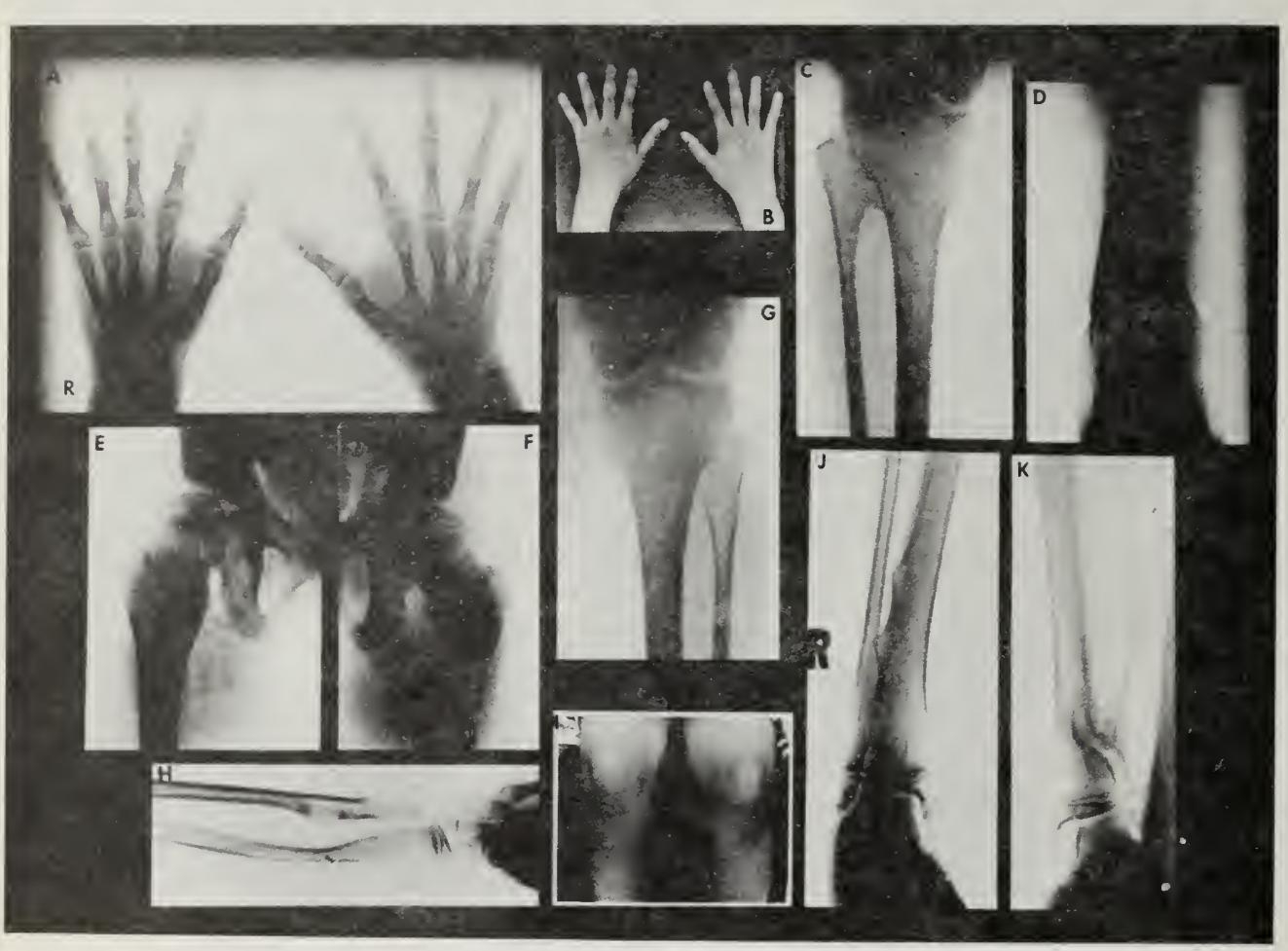


Fig. 2: *Caso 2 C.C.B. - B, I, Protuberancias óseas en dedos de la mano y rodillas. Encondromas - A- Falange 2 derecha. Exostosis - CD, H, J, K. E, F, deformidad del cuello del fémur. Característica de Metacondromatosis.*

de las manos y de los pies, y en los huesos largos. En la metacondromatosis se observan ambos tipos de lesiones y consecuentemente, la localización de las mismas puede ser tanto en los huesos largos como en las manos y los pies. Además, según Maroteaux (1), la metacondromatosis puede afectar pelvis, cuello del fémur y parte anterior de los cuerpos vertebrales.

Nuestros casos, según presentados en la Tabla I, muestran lesiones radiológicas de ambos tipos, y en los casos 1 y 2 se observan las lesiones características de pelvis y fémur ya mencionadas. El hecho de que en el caso 3 no se encuentren lesiones encondromatosas no invalida el diagnóstico, puesto que éstas tienden a desaparecer con el tiempo. En la exostosis múltiple hereditaria puede ocurrir una degeneración sarcomatosa, hecho que conlleva un pronóstico reservado. En la encondromatosis, las lesiones progresan de tal forma que las deformidades esqueléticas son harto frecuentes. En los casos estudiados por Maroteaux (1) y Lachman y cols (5) de metacondromatosis, las lesiones muestran una evolución benigna con regresión espontánea de algunas, como nosotros especulamos que sucedió en el caso 3 y, quizás, en su padre aunque ello no lo podemos afirmar ya que éste no estuvo disponible para nuestra evaluación.

En la metacondromatosis se ha observado un patrón de herencia autosómico dominante. Los antecedentes familiares en nuestros casos sugieren un patrón de herencia semejante ya que tenemos que se observan personas afectadas en cada generación, no hay problema de consanguinidad envuelto y los afectados tienen al menos uno de sus padres igualmente afectados.

Las peculiaridades que hemos reseñado de la meta-

TABLA I
HALLAZGOS RADIOLOGICOS

Tipo de Lesión	Caso 1. J. C. B.	Caso 2. C. C. B.	Caso 3, C. B. S.
EXOSTOSIS	Extremidad superior: ambos húmeros, proximal; radio derecho, distal; ulna izquierda, distal; metacarpo 1 derecho, proximal, medial; metacarpo 4 derecho, distal, lateral; metacarpo 3 izquierdo, distal, medial; falange 3 derecha, proximal y distal, lateral. Extremidad inferior: ambos fémures, distal; ambas tibias, proximal; ambas fíbulas, proximal y distal; metatarsos 4 y 5 izquierdos, distal, medial; falange 4 derecha, proximal, lateral; falange 3 izquierda, proximal, medial.	Extremidad superior: ambos húmeros, proximal; ambos radios, proximal y distal; ulna derecha, proximal y distal; ulna izquierda, proximal; metacarpo 3 derecho, proximal, medial; metacarpo 4 derecho, proximal, lateral; metacarpo 5 izquierdo, proximal, medial; falange 3 derecha, distal, medial; omoplato derecho, medial, superior. Extremidad inferior: ambos fémures, distal; ambas tibias, proximal; tibia derecha, distal; ambas fíbulas, proximal y distal.	Extremidad superior: ulna izquierda, distal. Extremidad inferior: fémur izquierdo, proximal y distal; fémur derecho, distal; tibia izquierda, proximal y distal; tibia derecha, proximal; fíbula izquierda, proximal y distal; fíbula derecha, proximal.
ENCONDROMAS	Extremidad superior: radio izquierdo, distal; falange 2 derecha, proximal. Pelvis: ambas crestas ilíacas, borde superior.	Extremidad superior: falange 2 derecha, distal. Extremidad inferior: cuello fémur derecho deforme.	No se encontraron.

condromatosis hacen imperativo un examen radiológico y genético detallado en todos los casos que presentan con lesiones sugestivas de exostosis múltiple hereditaria o encondromatosis. Solamente así se llegará al diagnóstico preciso.

Resumen

Hemos evaluado una familia donde la madre y sus dos hijas presentan con lesiones múltiples características de exostosis múltiple hereditaria y de encondromatosis. La asociación de estos hallazgos, y su patrón de herencia autosómico dominante, nos sugieren el diagnóstico de metacondromatosis, siendo ésta la primera descripción de esta condición en Puerto Rico y la caurta familia en el mundo.

Summary

We have studied a family in which the mother and



Fig. 3: *Caso 3 C.B.S. - A, B, C, D, E - Lesiones exostósicas, en fémures, tibias y fíbulas.*

two daughters present with the characteristic bone lesions of multiple hereditary exostosis and enchondromatosis. The finding of these lesions in association, as well as an autosomal dominant pattern of inheritance, suggests the diagnosis of metachondromatosis, being this the fourth family to be reported with this condition, and the first in Puerto Rico.

Reconocimientos

Deseamos expresar nuestra gratitud al Dr. Julio D. Mulero por referirnos los pacientes; al Sr. Angel L. Rivera por los estudios radiológicos, y a los Sres. José A. Rivera y Eugenio F. Bird por el trabajo iconográfico.

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NECROTIZING ENTEROCOLITIS

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Necrotizing enterocolitis is a serious and highly fatal condition of the newborn which is characterized by ischemic necrosis of the gastrointestinal tract. This disease was first reported by Genersich in 1891.

Since then the same entity had been periodically reported until 1964 when the first comprehensive report appeared from Babies Hospital. A recent report from the same hospital appeared in 1975 by Santulli and his group (3).

The purpose of this communication is to describe our recent experience in Puerto Rico with this disease entity.

Materials and Methods

The current presentation comprises 13 patients with necrotizing enterocolitis admitted to the Neonatal Intensive Care Unit of the University District Hospital from January 1974 through December 1975. During that period 12606 babies were admitted to the Nursery; 1517 were of low birth weight.

The records of all patients with necrotizing enterocolitis admitted to the Neonatal Intensive Care Unit of the University District Hospital were reviewed retrospectively.

The two main diagnostic criteria used to make the diagnosis were:

1. pathologic examination of surgical or autopsy specimen.
2. clinical disease including evidence of pneumatosis (intramural air) in X-rays.

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Results

Clinical Picture:

Sex:

There were five girls and eight boys (Table I). The incidence of low birth weight was 53 percent and sixty eight percent were premature (Tables I and II).

Perinatal Course:

The incidence of perinatal complications was high; seven had a history of maternal complications (Table III). Four had early neonatal complications which included respiratory distress syndrome, meconium aspiration syndrome and hemolytic disease of the newborn which required exchange transfusion in two babies.

Neonatal depression was found in 4 at one minute of age. Low Apgar persisted in two at five minutes of age (Table II).

Age of Onset:

Onset was usually in the first five days of life (8 patients). Four patients developed symptoms between 6 and 15 days and one at 6 weeks of age.

Relation to Feedings:

All patients had been fed prior to development of the disease. Standard newborn formula (17 calories per ounce) was given to the full term babies, ' SMA (24 calories per ounce) was given to the low birth weight infants.

Clinical Course:

The clinical disease was suspected because of abdominal distention and ileus in 11 patients. Guaiac positive or bloody stools were seen in 10 patients. Other clinical findings noted were peritonitis, per-

TABLE I
DISTRIBUTION BY SEX AND WEIGHT

SEX	
MALE	8
FEMALE	5
BIRTH WEIGHT IN GRAMS	
< 1500	3
1501 - 2500	4
> 2500	6

TABLE II
DISTRIBUTION BY GESTATIONAL AGE AND APGAR SCORE

GESTATIONAL AGE		
> 38 weeks		4
36 - 37 weeks		6
34 - 35 weeks		1
< 34 weeks		2
APGAR SCORE		
	1 MIN	5 MIN
⩾ 6	9	11
⩽ 5	4	2

TABLE III
COMPLICATIONS OF PREGNANCY AND DELIVERY

Placenta Previa	2
Intrauterine Asphyxia	2
Mother on Methadone	1
Neglected Transverse Lie	1
Premature Rupture of Membranes	1

foration, shock, hypoactivity, jaundice and vomiting (Table IV).

Laboratory and Bacteriology Findings:

Blood cultures were positive in 4 babies. Klebsiella was present in two of the four patients (Table V).

Cultures of the stool revealed significant microorganisms in ten babies: pure culture of Klebsiella in 6, Enterobacter in 2, Pseudomonas in 1 and Alkaligenes fecalis in one (Table V).

Radiographic Findings:

TABLE IV
PRESENTING SIGNS AND SYMPTOMS

Abdominal Distention	11
Bloody Stools	10
Sudden Shock	1
Others:	
Hypoactivity	6
Jaundice	4
Persistent Vomiting	3
Sclerema	1
Hypothermia	1
Bluish Discoloration of Umbilicus	1

TABLE V
CULTURES

BLOOD-KLEBSIELLA	1
KLEBSIELLA & ENTEROCOCCI	1
CITROBACTER	1
∝ ENTEROCOCCI	1
STOOL-(Predominant organism)	
KLEBSIELLA	6
ENTEROBACTER	2
PSEUDOMONAS	1
ALKALIGENES FECALIS	1

TABLE VI
MANAGEMENT OF INFANTS WITH NECROTIZING ENTEROCOLITIS AND THEIR SURVIVAL

	NUMBER	DIED	SURVIVED
CONSERVATIVE	9	5	4
SURGERY	4	3	1

Radiographic findings of pneumatosis intestinalis were present in eleven babies. The radiographic findings included: 1) intestinal dilatation, 2) pneumatosis (intramural gas) and 3) pneumoperitoneum.

Treatment:

Nine patients were treated medically, four survived, (Table VI). Their management included nasogastric decompression, intravenous fluid therapy and antibiotics. Radiographic studies were made every eight to twelve hours to detect the presence of intestinal perforation.

Four patients were operated upon, one survived. Surgery performed included resection of affected bowel and colostomy or ileostomy depending upon the site of involvement. The indication for operation was intestinal perforation proven by the finding of pneu-

moperitoneum in radiographic studies of the abdomen.

Pathologic Findings:

Autopsy was performed in five patients. Lesions were present in all parts of small and large intestine excluding duodenum. Multiple perforations of colon were found in three patients. Evidence of peritonitis was found in six patients either at post mortem examination or at surgery. One infant had perforated appendicitis with surrounding granulation tissue.

Discussion

A variety of factors have been implicated in the etiology of necrotizing enterocolitis ranging from ischemic damage to the intestinal mucosa to infection, exchange transfusions reactions to umbilical catheters and hyperosmolar formulas fed to small prematures.

Three factors appear to be essential in the development of the disease: injury to the intestinal mucosa, the presence of bacteria and the availability of a metabolic substrate such as hypertonic feedings.

Indirect injury to the mucosa may result from selective circulatory ischemia. This theory is based on the knowledge that stress produces marked vasoconstriction of the vascular bed of the skin, kidney and splachnic area, resulting in a redistribution of blood toward those organs (heat and brain) which would suffer irreversible damage if deprived of adequate perfusion. The stress may be from hypoxia, hypothermia, hypovolemia and low flow rate as in certain forms of congenital heart disease and from vasospasm or altered hemodynamics as a result of exchange transfusion or catheterization of umbilical vessels.

Factors which contribute to decreased enteric perfusion lead to a decrease in mucus production. The loss of the protective mucus exposes the mucosal cell to enzymatic digestion and permits bacterial invasion. Both substrate (formula feedings) and enteric bacteria are necessary for the production of hydrogen gas. The presence of hydrogen as intramural gas is responsible for the sequence of events which characterize the disease.

Klebsiella produces hydrogen gas; therefore, it may be significant that in six of thirteen patients there was intestinal colonization with Klebsiella. Frantz et al (3) reported an increased frequency of Klebsiella in stool cultures of patients with necrotizing enterocolitis as compared with controls. Bacterial colonization following naso-jejunal feedings has also been implicated as causing necrotizing enterocolitis.

Direct injury to the mucosa may be related to hyperosmolar feedings. There is evidence that hypertonic solutions alter intestinal perfusion. Book et al reported an increased incidence of necrotizing enterocolitis in small prematures fed a hypertonic elemental diet (4).

A series of experiments in an animal model have demonstrated the importance of stress, bacterial invasion and hyperosmolar feedings. The combination of these three factors helps to explain the fact that low birth weight infants are more susceptible to the disease. Sixty percent of our patients had intrauterine asphyxia. Furthermore the presence of confirmed bacterial sepsis in four patients indicates that bacterial invasion is an important etiologic agent. It has been found that formula feeding in conjunction with hypoxia produced enterocolitis in newborn rats and that breast feeding was completely protective. The important protective components of breast milk were the macrophages. Based on these findings small prematures are being fed breast milk in some institutions.

The incidence of necrotizing enterocolitis has been reported to be from 0.3 percent to as high as 7.5 percent in nurseries and intensive care units. In our Nursery 0.1 percent of all infants born in the hospital developed necrotizing enterocolitis. The true incidence is probably unknown.

In the 13 patients presented here there was evidence of necrotizing enterocolitis either by X-rays or pathologic findings. During that same period of time the disease was suspected, but not confirmed in twelve additional patients. They were treated promptly and did not develop clear evidence of pneumatosis.

In our group of patients only thirty eight percent survived. Survival rates have been reported ranging from 22 percent to 80 percent. One may speculate that survival of our infants might improve if cessation of feedings were instituted at the first suspicion of the disease.

Summary and Conclusions

The clinical picture of 13 infants with necrotizing enterocolitis is reviewed. The diagnosis was based on tissue examination in ten patients and clinical syndrome in three patients.

The importance of stress in the pathogenesis of

the disease is confirmed by high incidence of perinatal complications, particularly hypoxia seen in 60 percent of our patients.

Enteric bacteria seem to play an important role in the pathogenesis of the disease. Forty five percent of our patients had pure culture of Klebsiella in their stools.

The mortality was high in this group of patients. Improvement in survival may be expected by: (1) institution of early aggressive management in a premature infant who shows any abnormality of the gastrointestinal function, (2) close observation of infants at risk specially those with prematurity, intrauterine asphyxia, respiratory distress syndrome, sepsis and those requiring exchange transfusions, (3) aggressive medical treatment of those babies who develop evidence of abdominal distention with or without bloody stools. Close follow up of these infants with repeated radiographic studies of the abdomen must be done, (4) avoiding the use of elemental hypertonic formula in prematures which may contribute to produce the disease.

Resumen y Conclusiones

Se hace una revisión de las manifestaciones clínicas de enterocolitis necrotizante en trece lactantes. El diagnóstico se basó en el examen de tejidos en diez pacientes y en el síndrome clínico en tres pacientes.

Se confirma la importancia del stress en la patogenia de la enfermedad por la alta incidencia de complicaciones perinatales, particularmente de la hipoxia, que fue encontrada en el 60 por ciento de los enfermos.

Las bacterias entéricas parecen jugar un papel importante en la patogenia de la enfermedad. El cuarenta y cínco por ciento de los pacientes tenían coprocultivos positivos puros de Klebsiella.

La mortalidad en este grupo de pacientes fue alta. Podría esperarse una mayor supervivencia mediante: (1) la instauración precoz de medidas terapéuticas agresivas en el lactante prematuro que presente cualquier anormalidad de la función gastrointestinal (2) la observación cuidadosa de los lactantes en alto riesgo especialmente aquellos que son prematuros, están afectados por asfixia, tienen el síndrome de dificultad respiratoria, tienen sepsis y aquellos que sufran exanguineotransfusiones (3) terapéutica médica agresiva de los infantes que presenten evidencia de distensión abdominal con o sin melena; observación ulterior cuidadosa de estos mediante estudios radiográficos repetidos del abdomen (4) evitar la utilización de fórmulas elementales hipertónicas que puedan contribuir a producir la enfermedad en prematuros.

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PATRONES DE CRECIMIENTO INTRAUTERINO

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El concepto de peso al nacer en relación con la edad gestacional ha adquirido gran importancia práctica para el manejo del recién nacido, y en algunos casos de la madre del mismo. La disponibilidad de gráficas es escncial para evaluar el grado de crecimiento intrauterino.

El propósito de esta comunicación es actualizar los significados y definiciones de recién nacidos de distintos pesos y períodos de gestación, y proveer a los médicos puertorriqueños las gráficas esenciales para evaluar el crecimiento fetal.

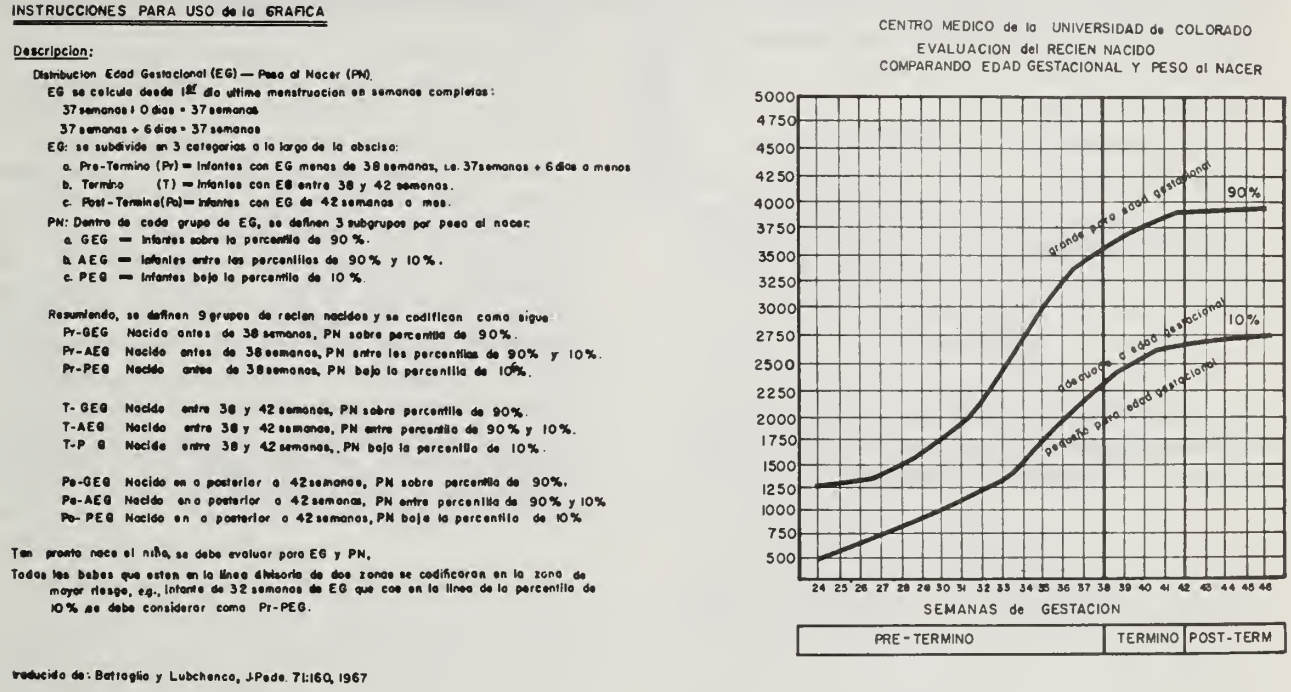
Tradicionalmente los infantes recién nacidos se clasificaban de acuerdo al peso de nacimiento. Todo recién nacido que pesaba menos de 2500 gramos (5 1/2 lb) se consideraba prematuro. Sin embargo se demostró que esta clasificación obscurecía diferencias importantes entre los infantes del mismo peso y diferentes períodos de gestación. No todos los infantes pequeños eran iguales y había diferencias en morbilidad y mortalidad entre ellos. En el 1950 el Comité de Expertos en Salud Materno-Infantil de la Organización Mundial de la Salud aconsejó que en vez de premadurez, se utilizara el término "Infante de Bajo Peso" para designar infantes con peso menor de 2500 gramos. El proceso de desarrollar estándares de crecimiento intrauterino es esencial pero difícil. Por necesidad se basa en el peso del infante al nacer y se acepta la premisa que el peso del infante pretérmino refleja crecimiento fetal normal en el útero. Al presente se han desarrollado estándares en Denver (Colorado) (1), Montreal (2), Oregon (3), Aberdeen (Escocia) (4) y por el Estudio Británico de Mortalidad perinatal (5-6). Las gráficas de Denver son las que más se han utilizado en los Estados Unidos. Se elaboraron en una población de clase socio-económica pobre que vive a una milla sobre el nivel del mar, por Lubchenco en 1963 (1) y correlacionan el peso del infante al nacer con la edad gestacional. (Fig. 1). En estas gráficas hay tres divisiones básicas: "pretérmino", "a término" y "postérmino". A término se refiere a los infantes nacidos entre 38 y 42 semanas de gestación. Se define como pequeño para el período gestacional al recién nacido cuyo peso está bajo la posición estadísticas porcentual (porcentil) de 10 a una edad gestacional específica. Este grupo de infantes presenta diferentes complicaciones y diferente pronóstico, dependiendo de la causa y el tipo del retraso de crecimiento.

Estas gráficas definen patrones normales de crecimiento intrauterino y proveen normas evaluativas del crecimiento posnatal de infantes prematuros. Permiten diferenciar el infante muy inmaduro del malnutrido en períodos de gestación extremos. Ambos están sujetos a riesgos altos de complicaciones, pero sus problemas en el período neonatal y más tarde en la vida son diferentes (Tabla I). En el período neonatal los infantes "pretérmino" van a sufrir predominantemente de dificultad respiratoria e hiperbilirubinemia. En los infantes de bajo peso por retraso del crecimiento intrauterino hay una incidencia alta de hipoglucemia. También presentan una incidencia elevada de anomalías congénitas debidas a aberraciones cromosómicas, como la Trisomía 18, y de infección intrauterina, como por ejemplo la producida por el sarampión alemán.

El peso del recién nacido con relación a su edad gestacional al nacer refleja el ambiente intrauterino y el efecto sobre su crecimiento prenatal de factores maternos tales como nutrición, toxemia y enfermedades crónicas. Pesos subnormales al nacer pueden ser indicio de gestación acortada o de un desarrollo inadecuado intrauterino.

Los problemas de los infantes de peso subnormal en estas dos categorías, los que nacen antes de tiempo y los que nacen a tiempo pero retrasados en su creci-

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INSTRUCCIONES PARA USO de la GRAFICA

Descripcion:

Distribucion Edad Gestacional (EG) — Peso al Nacer (PN).

EG se calcula desde 1er dia ultima menstruacion en semanas completas:
37 semanas + 0 dias = 37 semanas
37 semanas + 6 dias = 37 semanas

EG: se subdivide en 3 categorias a lo largo de la abscisa:
a. Pre-Termino (Pr) = Infantes con EG menos de 38 semanas, i.e. 37 semanas + 6 dias o menos
b. Termino (T) = Infantes con EG entre 38 y 42 semanas.
c. Post-Termino (Po) = Infantes con EG de 42 semanas o mas.

PN: Dentro de cada grupo de EG, se definen 3 subgrupos por peso al nacer:
a. GEG = Infantes sobre la percentila de 90 %.
b. AEG = Infantes entre las percentilas de 90 % y 10 %.
c. PEG = Infantes bajo la percentila de 10 %.

Resumiendo, se definen 9 grupos de recien nacidos y se codifican como sigue:
Pr-GEG Nacido antes de 38 semanas, PN sobre percentila de 90 %.
Pr-AEG Nacido antes de 38 semanas, PN entre las percentilas de 90 % y 10 %.
Pr-PEG Nacido antes de 38 semanas, PN bajo la percentila de 10 %.

T-GEG Nacido entre 38 y 42 semanas, PN sobre percentila de 90 %.
T-AEG Nacido entre 38 y 42 semanas, PN entre percentila de 90 % y 10 %.
T-P G Nacido entre 38 y 42 semanas, PN bajo la percentila de 10 %.

Po-GEG Nacido en o posterior a 42 semanas, PN sobre percentila de 90 %.
Po-AEG Nacido en o posterior a 42 semanas, PN entre percentila de 90 % y 10 %
Po-PEG Nacido en o posterior a 42 semanas, PN bajo la percentila de 10 %

Tan pronto nace el niño, se debe evaluar para EG y PN.

Todos los bebes que esten en la linea divisoria de dos zonas se codificaran en la zona de mayor riesgo, e.g., Infante de 32 semanas de EG que cae en la linea de la percentila de 10 % se debe considerar como Pr-PEG.

Traducido de: Battaglia y Lubchenco, J-Pede. 71:160, 1967

CENTRO MEDICO de la UNIVERSIDAD de COLORADO
EVALUACION del RECIEN NACIDO
COMPARANDO EDAD GESTACIONAL Y PESO al NACER

Figura 1

TABLA I
RIESGOS DE COMPLICACIONES EN LOS DIFERENTES PATRONES DE CRECIMIENTO INTRAUTERINO

Patrón de Crecimiento	Riesgos
Infantes pequeños para el período de gestación	1) Anomalías congénitas 2) Hipoglucemia 3) Deficit neurológico o mental
Infantes prematuros de tamaño adecuado para el período de gestación	1) Síndrome de dificultad respiratoria 2) Hiperbilirubinemia 3) Deficit neurológico o mental
Infantes grandes para el período de gestación	1) Hipoglucemia 2) Diabetes en la madre

miento, son muy diferentes. El pronóstico y los métodos de prevención están determinados por principios diferentes. En el caso de los prematuros hay que utilizar métodos para detener el parto y prolongar la estancia intrauterina o administrar drogas inductorias de la madurez de los órganos fetales. Para el infante con retraso del crecimiento intrauterino se necesita acelerar el crecimiento in útero de manera que el lactante nazca de tamaño normal.

Las gráficas proveen los medios de identificar los infantes grandes para el período de gestación, o sea, aquellos cuyo peso está sobre el porcentil de 90 en un período de gestación dado. Estos infantes pueden ser la primera manifestación de diabetes en sus madres y deben

vigilarse cuidadosamente ante la posibilidad de que desarrollen hipoglucemia en el período neonatal.

Las razones expresadas justifican ampliamente la clasificación de los recién nacidos utilizando las gráficas de crecimiento intrauterino.

Esto contribuirá a una atención más certera de los infantes de bajo peso al nacer y facilitará una clasificación estándar que podría ser utilizada como diagnóstico al implantarse los programas de auditoría médica en la Isla.

Apéndice

Las gráficas de crecimiento intrauterino fueron reproducidas con permiso del Editor de Pediatrics y de la doctora Lula Lubchenco (Pediatrics, 37: 403-408, 1966).

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DISCURSO DE TOMA DE POSESION COMO PRESIDENTE DE LA ASOCIACION MEDICA DE PUERTO RICO

Emilio A. Arce, MD

Como médico en el complejo ejercicio de la profesión, constituye un honor y un privilegio, asumir la presidencia de la Asociación Médica de Puerto Rico. Ciertamente estoy convencido que la labor que durante este año pueda desempeñar depende no sólo del entusiasmo, dedicación y esfuerzo que estoy dispuesto y que habré de realizar, sino también debe y tiene que apoyarse en la colaboración íntima de los organismos directivos de nuestra entidad y en la labor de cada uno de los compañeros asociados.

Estamos conscientes de la responsabilidad que conlleva presidir esta Asociación Médica y de las complejidades del presente y del futuro inmediato, pero estamos seguros de que con la ayuda de ustedes cumpliremos nuestras metas a corto y a largo plazo.

Es significativo y motivo de gran regocijo que durante nuestra incumbencia se cumplirán setenta y cinco años de haberse fundado la Asociación Médica de Puerto Rico. Setenta y cinco largos y fecundos años de servicio a la comunidad y a la profesión médica, oportunidad ésta que debemos aprovechar para desarrollar aquellas actividades que puedan contribuir a fortalecer aún más la imagen de nuestra profesión y de nuestra institución. Consideramos que la importancia de esta efeméride nos debe llevar a la evocación de nuestros fundadores y de nuestros Pasados Presidentes, muchos de los cuales aún están activos en su quehacer profesional.

Hemos tenido a bien nombrar un Comité Especial, Comité 75, que habrá de desarrollar durante todo este año diversas y variadas actividades de índole educativa, cultural, de servicio a la comunidad y de tipo profesional que den marco adecuado al Aniversario de Diamante de nuestra Institución.

Nos ha tocado vivir una era llena de retos y de constantes cambios en el diario quehacer de nuestra profesión. La Educación Médica Continuada tiene ya entre nosotros un alto sitial; y es una de las prioridades en la que estamos comprometidos. Para poder ofrecer a toda nuestra membresía las máximas facilidades para cumplir con los requisitos de contínua educación hemos de aunar esfuerzos con los Programas de Educación Médica Continuada que proyectan varias entidades educativas, a saber: Escuela de Medicina de la Universidad de Puerto Rico, Hospital de Veteranos, Hospital de la Capital y los distintos Distritos y Secciones de Especialidades que componen nuestra Asociación. No descansaremos hasta ver plasmado en realidad el que nuestros médicos tengan acceso a suficientes cursos que les permitan cumplir con lo exigido, sin tener que salir de Puerto Rico.

Consideramos que ha llegado el momento de una evaluación profunda y exhaustiva de las necesidades reales de nuestra Isla en cuanto al número de escuelas de medicina necesarias para egresar los médicos que realmente se necesitan en el Puerto Rico de hoy y del mañana, siempre sobre bases de alta calidad. De nada valdría el esfuerzo de todos los que de una forma u otra están envueltos en estos programas de alta Educación Médica, si no se cumple con la formación de médicos de excelencia.

A este respecto estableceremos el diálogo necesario con las personas preocupadas en este tema: Rectores y Decanos, miembros del Consejo de Educación Superior, Secretario de Salud y otros, a fin de aportar nuestras opiniones en esta problemática que debe ser resuelta en un futuro inmediato.

Igualmente no podemos mantenernos ajenos a los dramáticos cambios socio-económicos que afectan a Puerto Rico, y en esta fase es donde más tenemos que trabajar para entender y tratar de resolver la problemática de las nuevas características del desarrollo urbano e industrial de Puerto Rico en términos de la salud mental — altísima prioridad de nuestro pueblo — y de la salud física de cada puertorriqueño. En este aspecto intensificaremos al máximo nuestro intercambio de ideas con el Gobierno y con otros sectores de la comunidad para captar, interpretar y transmitir el mensaje más favorable a la salud de nuestro pueblo.

Estamos seguros que la nueva Administración que asumirá el poder el próximo 2 de enero, habrá de concederle a los servicios médico-hospitalarios la prioridad que éstos merecen dentro del marco de la libre selección de médicos y hospitales, y esperamos la especial coo-

peración a este respecto del Dr. Jaime Rivera Dueño.

Entre las otras áreas que requieren mayor trabajo durante el año que iniciamos hoy, figuran nuestras relaciones con todos los profesionales que integran el equipo de la salud. Debemos lograr aunar los pensamientos, las metas y los esfuerzos de muchos puertorriqueños pensantes y preocupados. Es necesario reactivar, y a ello nos comprometemos, el Concilio de Salud de Puerto Rico, en el que estarán representadas todas las profesiones que integran el componente de la salud.

Es imperativo que redoblemos energías para mejorar nuestra comunicación interna y nuestra proyección hacia la comunidad. Fortaleceremos los Distritos existentes y trataremos de que se organicen otros en aquellas áreas donde nuestros médicos así lo interesen.

Brindaremos especial consideración al concepto que se conoce como "Agencia de Sistema de Salud". Hemos de estrechar los lazos con los estudiantes de medicina, internos, residentes y muy en especial con los compañeros que ejercen su profesión en el sector gubernamental, para juntos tratar de lograr que se mejoren sus condiciones de trabajo.

Concederemos especial atención a los Programas Medicare y Medicaid, en lo que respecta a su implementación y utilización; y junto a nuestro Gobierno nos esforzaremos para que se aumente la aportación federal en el Programa Medicaid a fin de que Puerto Rico reciba lo que en justicia le corresponde.

En el área de la legislación estaremos muy al tanto de lo que habrá de ocurrir con la Ley Núm. 11 del 23 de junio de 1976, así como con la Ley Núm. 74 relacionada con el Seguro de Responsabilidad Profesional. Es innegable que ambas leyes requieren enmiendas sustanciales. Igualmente, a través del Consejo de Política Pública, impulsaremos una serie de proyectos en beneficio de la comunidad, entre ellos el que los gastos de seguro médico-hospitalario puedan ser deducibles de la contribución sobre ingresos; que se aumente la aportación patronal en el seguro médico-hospitalario de los empleados públicos, y que el aumento se haga por niveles de ingreso con una mayor aportación para las escalas de ingreso más bajas; que los empleados de salud de los Gobiernos Municipales y hospitales estatales reciban igual remuneración por servicios análogos.

Entiendo que debemos fomentar aún más la labor de discusión de ideas en el seno de nuestra Asociación, sin que las discrepancias de criterios afecten nuestra solidaridad grupal y nuestra unidad profesional para el bien de Puerto Rico. Es inaplazable redoblar energías para orientar e informar a la comunidad sobre lo que es la Asociación y lo que es la profesión médica, de manera que logremos aclarar los equívocos y ataques demagógicos que en ocasiones se han hecho contra nosotros. Para ello necesitamos un frente común, un sólo techo, que nos permita contrarrestar cualquier clase de intento por socavar nuestra cohesión y nuestras estructuras.

La profesión médica es sacrificio, vocación y obra de amor al prójimo. Por eso debemos sentirnos orgullosos de ejercer esta noble profesión, cumplir los postulados que la guían y pertenecer a la Asociación Médica de Puerto Rico. Nuestro objetivo principal como profesionales y como Institución ha sido, es y debe ser siempre, brindar el mejor servicio y atención a nuestros pacientes y la solución de los problemas médico-hospitalarios de nuestro país.

He nombrado en mi equipo de trabajo profesionales que integran el ayer y el mañana de nuestra Asociación, de tal forma que nuestra Institución tenga el sabio consejo de los experimentados y la nueva vitalidad de hombres y mujeres que se han destacado por su interés en servirle bien a nuestra Asociación y por ende a toda la membresía, y al pueblo de Puerto Rico. Sé que con este grupo de consejeros hemos de conseguir que nuestra Asociación continúe pujante y sólida, hacia nuevas metas.

Con el nuevo Reglamento, en parte ya aprobado, y espero que en su totalidad en enero de 1977, bregaremos de una mejor forma con los problemas y con el servicio que entendemos estamos obligados a brindar a nuestra membresía; a la par estamos implementando una re-estructuración de nuestro personal administrativo con el único propósito de brindar un mejor servicio.

Al agradecer a ustedes la confianza que han depositado en mi persona para dirigir nuestra querida Institución, les exhorto a defenderla, amarla y a ofrecerle todo vuestro respaldo, vuestra mejor voluntad y entusiasmo. Solo así podremos conseguir que seamos respetados y entendidos. Nos animan los mejores propósitos de dialogar con todos los compañeros médicos. Entiendo que la mejor forma de progresar como entidad es la de discutir problemas y buscar soluciones realistas y beneficiosas. Todos constituímos la Asociación Médica de Puerto Rico. Por tal razón es que, repito, la misión es de todos y no solamente de los que formamos parte de los Cuerpos Directivos de esta Institución.

Para terminar, deseo saludar en forma de agradeci-

miento al compañero Presidente Saliente, Dr. Luis A. Viñas Sorbá, por su eficiente labor y grandes desvelos en beneficio de nuestra organización, y ofrecerle la bienvenida al Presidente Electo, Dr. Rafael Berríos Martínez, quienes estoy seguro me ayudarán a convertir en realidad los propósitos que nos animan en nuestra gestión presidencial..

Que Dios nos ayude a todos a continuar la trayectoria de los fundadores y Pasados Presidentes de esta Institución para convertir en realidad nuestros más caros anhelos de servirle cada vez mejor al pueblo de Puerto Rico como profesionales y como Institución.



DR. EMILIO A. ARCE

Presidente, Asociación Médica de Puerto Rico

1976

Nació el doctor Arce en Santurce, Puerto Rico el 15 de enero de 1932. Realizó sus estudios de Escuela Superior en la Escuela Superior Central de Santurce, donde se graduó en el 1948, pasando a la Universidad de Oklahoma donde hizo sus estudios de premédica.

Sus estudios profesionales los realizó en la Universidad de Salamanca, España, en la cual obtuvo su licenciatura en medicina y cirugía en el año 1957.

Su entrenamiento postgraduado de Internado Rotativo lo realizó en el Hospital de Distrito de Fajardo y en el Hospital Presbiteriano de Santurce.

Realizó estudios postgraduados de Oftalmología en la Universidad de Barcelona y en la Escuela de Medicina de Puerto Rico, Departamento de Oftalmología, bajo el Dr. Guillermo Picó, terminando su entrenamiento como Oftalmólogo en el año 1948 y en los próximos cinco años estuvo a cargo de un Programa Federal de Servicio e Investigación en Glaucoma en el Hospital Universitario del Recinto de Ciencias Médicas.

Igualmente en los últimos nueve años ha prestado sus servicios al Fondo del Seguro del Estado como Médico Consultor.

Es miembro, entre otras, de la Asociación Médica Americana, de la Sección de Oftalmología de la Asociación Médica de Puerto Rico, de la Asociación Panamericana de Oftalmología, de la Asociación Americaua de Oftalmología, de la Sociedad Española de Oftalmología, y ha presidido numerosos Consejos y Comités de la Asociación Médica de Puerto Rico, de la Asociación de Puertorriqueños Graduados en Universidades Españolas, del Instituto Puertorriqueño de Cultura Hispánica y de la Sociedad Médica del Distrito Este, la cual presidió en el año 1972.

NOTICIAS

FROM THE AMERICAN SOCIETY OF CONTEMPORARY OPHTHALMOLOGY

FIRST INTERNATIONAL GLAUCOMA CONGRESS

The world's leading medical authorities on glaucoma will lecture on their latest research findings at the First International Glaucoma Congress, January 31-February 1, 1977, at the Diplomat Hotel, Hollywood, Florida. The glaucoma congress is being held in conjunction with the 12th Annual Scientific Assembly of the American Society of Contemporary Ophthalmology January 30 through February 5 at the same site. The Congress is sponsored by Lederle Laboratories.

The glaucoma congress will be under the honorary chairmanship of Dr. Bernard Becker, of Washington University, St. Louis, recognized as a pioneer in glaucoma research. Authorities in other areas of ophthalmic research are scheduled to conduct seminars during the week-long meeting: Cornea-External Diseases, Dr. Claes Dohlman, Harvard Medical School; Cataract, Dr. David Paton, Baylor University Medical School; Vitreous-Choroid-Retina, Dr. Harvey Lincoff, Cornell University Medical School; and Oculoplastic Surgery, Dr. Pierre Guibor, Doctors Hospital, New York, N. Y.

A series of tutorials and workshops will be offered in Microsurgery, Phakoemulsification, Oculoplastic Surgery, Vitrectomy, Fluorescein Angiography, Gomioscopy, Ultrasonic Evaluation of the Eye, External Ocular Disease, Intraocular Lens Technology, and Malpractice. The program meets the criteria for 42 hours of credit in Category I for the Physician's Recognition Award of the American Medical Association and for the ASCO Certificate of Advanced Studies in Ophthalmology.

For further information: Dr. John Bellows, Director, ASCO, 6 North Michigan Avenue, Chicago, Illinois 60602.

HEW NEWS:

Beginning in January 1977, a person who goes to the hospital under Medicare will be responsible for the first $124 of his hospital bill. The present deductible of $104 will remain in effect for Medicare hospital admissions during the rest of 1976.

In announcing the new $124 deductible, James B. Cardwell, Commissioner of Social Security, noted that the law requires an annual review of hospital costs under Medicare and an adjustment of the portion of the bill for which a Medicare beneficiary is responsible, if these costs have risen substantially. The law provides a formula for determining the amount of any adjustment in the deductible amount.

Commissioner Cardwell said the increase in the deductible results from continuing increases in hospital costs. He pointed out that hospital costs have been increasing over twice as fast as the overall cost-of-living and said that these inflationary increases in hospital costs are largely responsible for the 19 percent increase in the inpatient hospital deductible.

The hospital deductible amount, Commissioner Cardwell explained, is intended to make the Medicare beneficiary responsible for expenses approximately equal to the average cost of one day of hospital care. At the present time the average hospital stay under Medicare costs about $1,600.

Mr. Cardwell said that when the hospital deductible amount changes, the law requires comparable changes in the dollar amounts that a Medicare beneficiary pays toward a hospital stay of more than 60 days, or a posthospital extended care stay of more than 20 days.

When a Medicare beneficiary has a hospital stay of more than 60 days, he will pay $31 a day for the 61st through the 90th day, up from the present $26 per day. Should a beneficiary wish to draw on his "lifetime reserve" days, the extra 60 hospital days a beneficiary can use when he needs more than 90 days of hospital care in a benefit period, he will pay $62 for each reserve day used, instead of the present $52 per day.

If he has a posthospital stay of over 20 days in a skilled nursing facility, he will pay $15.50 per day toward the cost of the 21st day through the 100th day, up from the present $13 per day.

About 24.7 million persons are covered by hospital insurance under Medicare in 1976 and this number will increase to 25.3 million persons in 1977. The cost of Medicare hospital insurance is expected to increase from $13.6 billion in 1976 to $16.1 billion in 1977.

The basic premium paid by Medicare beneficiaries for their supplementary medical insurance coverage will increase from the present level of $7.20 a month to $7.70 a month for the 12-month period beginning next July.

The supplementary medical insurance program, also known as Part B, complements the basic hospital insurance part of Medicare by helping to pay physicians' bills and a wide variety of other medical expenses in and out of the hospital. The costs are shared by the participants and the Federal Government.

About 25.4 million persons will be enrolled in the supplementary medical insurance part of Medicare in fiscal 1978, including 2.5 million disabled persons under 65.

HEW Secretary David Mathews said the law requires him

to review in December the cost of the supplementary medical insurance program and to set a premium rate which, together with the Federal contribution, is estimated as sufficient to cover all expenditures that will be incurred in the 12 months beginning July 1, 1977.

The law also requires that any increase in the premium amount next July 1 must be limited to the percentage by which social security cash benefits increased in 1976.

"Social security benefits increased by 6.4 percent in June 1976, while the cost of supplementary medical insurance is increasing by more than 20 percent a year," the Secretary said. "As a result, the premium must increase by 6.4 percent under the law. The mathematics produces a premium rate rounded to $7.70 a month, effective July 1, 1977."

The effect of this limitation is that premium income from the aged and disabled will cover 28 percent of the costs of supplementary medical insurance from July 1977 to June 1978, while the Federal government will pay a 72 percent share.

The cost of benefits under the supplementary medical insurance program is expected to increase from about $6 billion in fiscal 1977 to $7.4 billion in fiscal 1978, the Secretary said. The major factors are a projected increase in physician's fees recognized by Medicare, increases in the number of services rendered, a trend toward more expensive services, and an increase in the cost and use of hospital outpatient services.

Some Part B beneficiaries pay more than the basic premium because they enrolled late or because they withdrew and then re-enrolled. Their premiums also will increase beginning July 1, 1977.

FROM THE AMERICAN MEDICAL ASSOCIATION - AMA PUBLIC AFFAIRS DIVISION MEMO

TO: Executive Directors
State Medical Societies
Metropolitan County Medical Societies
National Medical Specialty Societies

SUBJECT: Editorial on Fraud and Abuse

Here is a suggested editorial for your journal or bulletin. It focuses upon the frustrating problem of Medicaid-Medicare fraud and abuse that have received extensive press attention in recent months.

The editorial points out steps that the AMA and the Federation have taken to alleviate the problem and calls for continued concerted action directed toward further curbing fraud and abuse.

EDITORIAL

Our profession today is being smeared by a brush that has gone haywire.

We have called and worked for crackdowns on Medicaid-Medicare fraud and other abuses of our ethical standards—yet we are being tainted with "guilt by association" simply because the abusers include doctors.

While political hay is being made out of the abuses, our efforts against them are mostly ignored and even circumvented by politicians. Judicial roadblocks also have been placed in our way.

The House of Delegates of the American Medical Association, at its convention last June, urged government agencies to prosecute Medicaid-Medicare defrauders with due speed and offered the Association's cooperation.

HEW has set up a special fraud office, and Congress this autumn provided for an Inspector General of all HEW programs, particularly Medicaid. But how effective can government be, aside from finger-pointing at the Medicaid-provider incomes and televising its fists?

Well, Senator Sam Nunn (D.-Ga.) recently expressed the belief that fraud is "pervasive at all levels" of Medicaid administration, including HEW's program to detect it.

James H. Sammons, M.D., executive vice-president of the AMA, has bluntly stated:

"We are tired of doctors being made the whipping boy by publicity-seeking bureaucrats and politicians. If they want to clean up Medicare and Medicaid, let them go after the unscrupulous operators of Medicaid "mills" and that small percentage of equally unconscionable nursing home operators who prosper in every major city with political protection. They are at the root of the corruption and the fraud and abuse."

The AMA has equipped state medical societies with two pieces of model legislation to toughen the disciplinary powers of state licensing boards. How many states have adopted them?

Even so, license revocations and other disciplinary actions reported by state medical boards jumped from 179 in 1974 to 246 in 1975 to 335 in the first eight months of 1976, according to the boards' national federation. And, for the most part, there are only M.D.'s on those boards.

Physician members of the PSRO in New York County have tried to use powers conferred by the PSRO law to control Medicaid-mill abuses. But their efforts have been stymied by state and city officials or by the courts.

Some politicians choose to be unaware that medical societies have conscientious, stringent committees on credentials, grievances, and ethics.

Let's work as best we can with government and insurance carriers to show our concern—and to push for a cleanup.

ANNOUNCEMENT OF MEDICARE HOSPITAL INSURANCE DEDUCTIBLE AND COINSURANCE FOR 1977

The Secretary of Health, Education, and Welfare has announced that the inpatient hospital deductible under Part A of Medicare will be increased from $104 to $124 for benefit

periods *beginning* in 1977. Notice of the $124 deductible and related coinsurance amounts has been published in the Federal Register.

Under Section 1813 (b) (2) of the Social Security Act, as amended, the Secretary is required to make an annual review of hospital insurance costs under Medicare and, if necessary, to adjust the deductible and related coinsurance amounts for the following calendar year. The formula in the law requires that the deductible be based on $40 times the ratio between the average per diem hospital cost for insured persons under the program in 1975 and the corresponding average in 1966, rounded to the nearest multiple of $4. These averages were $117.65 and $37.92 respectively, with a ratio of 3.103. When this ratio is multiplied by $40, the result is $124.12, which must be rounded to $124, the nearest $4 multiple.

The law also specifies that coinsurance amounts must be proportionate to the inpatient hospital deductible. Thus, for benefit periods starting in 1977, the deductible amount for the first 60 days of inpatient hospital care will be $124; the hospital coinsurance amount for the 61st through 90th day of each benefit period will be $31 a day (1/4 of the deductible); and the hospital coinsurance amount for each lifetime reserve day used will be $62 a day (1/2 of the deductible). For the 21st through 100th day of services in a skilled nursing facility, the coinsurance amount for benefit periods starting in 1977 will be $15.50 a day (1/8 of the deductible).

The new amounts are effective only with benefit periods *starting* in 1977. The current $104 inpatient hospital deductible and related coinsurance amounts remain in effect for benefit periods which start in 1976, even though the benefit period extends into 1977.

CHILDREN'S HOSPITAL NATIONAL MEDICAL CENTER AND GEORGE WASHINGTON UNIVERSITY are sponsoring a three day Symposium on Common Pediatric Problems on June 8-10, 1977, which may be of interest to our membership. It features a Symposium on Hematology, Oncology and Immunology; a Symposium on Adolescence; and a day of workshops.

Further information may be obtained by writing to Mrs. Susan Weiss, 13407 Brackley Terrace, Silver Spring, Md. 20904.

CARE-MEDICO NEEDS VOLUNTEERS FOR SHORT-TERM DUTY OVERSEAS

Medical specialists are urgently needed as volunteers in overseas programs conducted by MEDICO, a service of CARE.

Donating a month or more of their time and skills, physicians help train young men and women in their particular branch of medicine or surgery.

Openings are available in Afghanistan, Bangladesh, Dominican Republic, Indonesia, Jordan, Nicaragua and Tunisia.

Volunteers pay their own costs of travel and maintenance which may be tax deductible.

For further information, phone (202) 223-2277 or write George B. Mathues, Director, MEDICO Volunteer Specialists, 2007 Eye Street, N. W., Washington, D. C. 20006.

A N U N C I O S

OFICINAS MEDICOS – ALQUILER O VENTA

Próximas a Hospital Presbiteriano, 1,100 pies cuadrados. Planta baja Lobby del Condominio Condado Ambassador, Ashford 1407. Muy bien decoradas, parking disponible. Información Srta. Berríos 767-1371, 1350 y 1321.

PARA LA VENTA

Oficina en Edificio First Federal de Río Piedras de 500 p/c para $30,000. Oficina de 2,000 p/c en Calle Parque, Pda. 23, y otra de 4,000 p/c en Pda. 23 en Ponce de León, propias para Laboratorio Clínico u oficinas de médicos. Dos edificios en Hato Rey, buenos para vender en apartamientos y hacer magnífica ganancia doblando su inversión. Otras propiedades. Para más información, llame a José Arsuaga, Tel. 765-9494.

APERTURA DE CLINICA

El Centro Siquiátrico de Puerto Rico les anuncia la apertura de una moderna clínica "Habit Modification Clinic".

Es una división adscrita al centro que ofrecerá tratamientos para ayudar a las personas a controlar hábitos mal adquiridos tales como:

a. beber o fumar en exceso
b. controlar el peso (obesidad)
c. evaluaciones psicológicas y sicométricas
d. corregir malos hábitos de estudio

Si tienes interés y verdadero deseo de cambiar tus hábitos y por consiguiente tu personalidad solicita nuestros servicios. Centro Siquiátrico de P. R., tel. 783-0610.

AGRADECIMIENTO

En este año a punto de terminar, la Junta Editora desea expresar su más profundo agradecimiento a todos los patrocinadores del Boletín de la AMPR, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos.

La Junta Editora desea expresar igualmente su agradecimiento a los siguientes compañeros médicos que durante el año que termina nos han brindado su desinteresada ayuda y colaboración en la evaluación de los artículos que se nos han sometido. La ayuda brindada por estos compañeros ha permitido una revista de actualidad que refleje la calidad de la medicina puertorriqueña.

Para todos, nuestro más profundo agradecimiento.

Pablo I. Altieri, M. D.
Juan M. Aranda, M. D.
Conrado Asenjo, M. D.
Robert Axtmayer, M. D.
Ramón H. Bermúdez, M. D.
Rafael Burgos Calderón, M. D.
Guillermo Cintrón, M. D.
Angel A. Cintrón Rivera, M. D.
Arsenio Comas Urrutia, M. D.
Nelson Fernández Blasini, M. D.
Edmundo Figueras, M. D.
Ramón E. Figueroa Lebrón, M. D.
Juan C. Figueroa Longo, M. D.
Herman J. Flax, M. D.
Roberto Fortuño, M. D.
José M. García Castro, M. D.
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Pedro H. García Pont, M. D.
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Eduardo Mirabal Fort, M. D.
Manuel N. Miranda, M. D.
Francisco Olazábal, M. D.
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Guillermo Picó, M. D.
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Rafael Villavicencio, M. D.